An Investigation of Long-Term Forgetting in People with Temporal Lobe Epilepsy

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Main Research Project

An Investigation of Long-Term Forgetting in People with Temporal Lobe Epilepsy

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Abstract

Temporal lobe epilepsy (TLE) is a form of epilepsy characterised by focal seizures within the temporal lobes. It is well known that associated temporal lobe structures are implicated in the acquisition and consolidation of new declarative memories. Therefore, it is unsurprising that people with TLE often complain of memory difficulties. However, measures that are used currently clinically to assess for the presence of memory deficits do not always detect evidence of memory difficulties in this population. In the past, this discrepancy has been interpreted as evidence of low mood in those who present with subjective difficulties. Recently, it has been suggested that people with TLE may experience a phenomenon known as 'accelerated long-term forgetting' whereby acquisition and retention of declarative memories over initial consolidation delays (i.e. approximately 30 minutes) is intact but then rapidly forgotten over longer timeframes of hours, days, or weeks: outside the timeframe of current standardised memory measures. Although this may provide an explanation for why memory problems in the population with TLE currently go largely undetected, the research in this area has typically been methodologically flawed. Therefore, the aim of the current study was to investigate whether people with TLE still exhibit evidence of accelerated long-term forgetting after controlling for the methodological confounds of previous research. Eighteen participants with TLE and eighteen neurologically healthy controls were assessed for long-term forgetting using two novel measures designed for the purpose of the current study to meet a number of methodological criteria. Each group was matched for age, education and intelligence and performance on standardised memory measures was comparable. Evidence for accelerated long-term forgetting at one-week delay was found for the verbal task but not for the visuo-spatial task, where accelerated forgetting occurred at medium-term delay. Consideration of possible variables important in forgetting rates was conducted through exploratory analyses, which cautiously implicated mood, mesial temporal lobe pathology, polytherapy, and laterality of seizure focus in accelerated forgetting in the two measures differentially. The implications of these findings were discussed and recommendations for future research suggested.

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1. Introduction

This chapter begins with a description of the principle theories of memory and declarative memory consolidation. It then moves to discuss how these theories relate to the phenomenon of accelerated long-term forgetting and how the study of accelerated long-term forgetting could provide important theoretical insights into the current memory consolidation models. The chapter then introduces a definition of epilepsy, and particularly describes temporal lobe epilepsy (TLE). Long-term forgetting has commonly been investigated in this population and the possible aetiologies for findings of accelerated forgetting are discussed. Finally, the chapter critiques the methodological constraints of the long-term forgetting literature currently and presents the rationale for the current study, including a summary of the aims and hypotheses.

For the purpose of consistency regarding the interval following which recall is tested in the current study and the wider forgetting literature: 'short-term' will be used to denote recall assessed following immediate learning, i.e. 0- to 30-seconds; 'medium-term' will be used to denote recall assessed at delays traditionally assumed to be sensitive enough to detect adequate retention of material, i.e. 10-minutes to one-hour; and 'long-term' will be used to denote recall assessed at least one-day after initial learning and can include recall at delays of up to eight weeks. These terms are not necessarily indicative of the timeframe over which memory consolidation occurs, which has also differentiated between 'short-term' and 'long-term' and may reflect different entities. The use, currently, of these terms in relation to testing interval is simply a way to categorise the delay intervals researchers have typically used in forgetting studies.

1.1 Theoretical Models of Memory and Declarative Memory Consolidation

Declarative memory is defined as the conscious memory for facts and events (Squire, Stark & Clark, 2004). The concept of memory consolidation refers to the process of transferring newly registered information into a more permanent memory store, and contemporary views often define consolidation according to different levels of analysis. Consolidation can reflect: (i) neurobiological processes,

i.e. the synaptic modification of neural networks that occur whilst learning (e.g. Bailey & Chen, 1983; Tully, Preat, Boynton & Del Vecchio, 1994); (ii) system processes, i.e. the reorganisation of mesial temporal and neocortical structures in response to new information (e.g. Alvarez & Squire, 1994; Nadal & Moscovitch, 1997); and (iii) time-dependent processes, during which a memory trace establishes permanence within a non-specified brain network (e.g. Karni, Tanne, Rubenstein, Askenasy & Sagi, 1994). These levels typically operate over different timeframes whereby synaptic consolidation occurs over minutes to hours after learning whilst systems consolidation takes much longer (Dudai, 2004).

1.1.1 Modal Model

Atkinson and Shiffrin (1968) proposed a three-part modal model of memory, whereby information is first registered using the senses, then transferred to a short-term store, and from there to a possibly permanent long-term store relatively rapidly. The sensory register was posited to detect and hold information for use in short-term memory, and included both iconic memory, associated with the visual system (Sperling, 1960; Coltheart, Lea & Thompson, 1974), and echoic memory, associated with the auditory system (Darwin, Turvey & Crowder, 1972; Glucksberg & Cowan, 1970). The information attended to in the sensory register then entered the short-term store, and could be held in this store for approximately 30 seconds (Posner, 1966). Information was then postulated to transfer from the short-term store to a relatively permanent long-term store relatively automatically, providing it was attended to sufficiently in the short-term store (Parkin, 1993). This transfer of information has typically been assumed to involve a single-stage consolidation process (Weingartner & Parker, 1984). The long-term store was theorised to be limitless in duration and capacity.

Support for this model was provided at the neurobiological level (e.g. Hebb, 1961), and from patient lesion studies, which suggested there was a distinction between short-term and long-term memory (e.g. Scoville & Milner, 1957; Milner, 1966). However, this modal model has also received criticism. Many concepts of the model are poorly defined and do not accurately predict theoretical concepts (Tarnow, 2010). Additionally, it does not account for demonstrations of impaired working (short-term) memory in the context of relatively preserved episodic long-

term memory, as demonstrated in other patient lesion case studies (e.g. Shallice & Warrington, 1970). These studies have also shown that memory consolidation does not occur as a single-stage, automatic, process (Frankland & Bontempi, 2005).

Although this model provided a theoretical distinction between 'short-term' and 'long-term' memory that has prevailed to the current day (Jansari, Davis, McGibbon, Firminger & Kapur, 2010), it does not adequately explain the process of memory consolidation and has traditionally viewed 'long-term' memory as measurable relatively soon (i.e. minutes) after initial learning. The models presented in the remainder of this section provide a more comprehensive account of memory consolidation, based on system processes.

1.1.2 Simple Network Model

Alvarez and Squire (1994) proposed a 'simple neural network model', also known as the 'standard model' (Nadal & Moscovitch, 1997), involved in the consolidation of declarative memory. The mesial temporal lobe (MTL) has been found to be implicated in declarative memory processes (Schacter, 1987; Squire, 1987; Schacter & Tulving, 1994), and includes the hippocampal region and adjacent cortical areas of the entorhinal, perirhinal, and parahippocampal cortices. Alvarez and Squire posited that initial memory consolidation relies on regions within the MTL, but that secondary consolidation processes additionally occur, during which memories gradually become independent from MTL structures. They suggested that the neural substrates of more permanent memories gradually change or reorganise over time, shifting from the MTL laterally to the neocortex (Squire, 1987; Mishkin, 1982; Damasio, 1989; Milner, 1989).

Their model of consolidation can be summarised in five statements: (i) the interaction between multiple, separated, areas of the neocortex and MTL are crucial for the formation, consolidation and retrieval of long-term declarative memory; (ii) the entorhinal cortex acts as a mediator between the hippocampus and other MTL structures (i.e. perirhinal and parahippocampal cortices), which in turn communicate with the neocortex; (iii) key to consolidation within the neocortex is the gradual binding together of multiple cortical connections that, as a whole, store representations for the declarative memory; (iv) the MTL has limited

capacity but learns rapidly whilst the neocortex has a large capacity but learns slowly; and (v) repeated reactivation between the MTL and neocortex strengthens connections among cortical sites, eventually fully establishing the memory within the neocortex and eliminating the need for MTL co-activation. Alvarez and Squire (1994) reported a computational model that provided support for their proposal, and replicated behaviour observed in lesion experiments.

The premise of this model was based on findings that damage to MTL structures resulted in a temporal gradient of retrograde amnesia (Zola-Morgan, Squire & Amaral, 1986; Winocur, 1990; Kim & Fanselow, 1992; Cho, Beracochea & Jafard, 1993), whereby remote memories were relatively spared after damage to the MTL, whilst more recent memories were typically impaired. This suggested that MTL structures were not necessary for remote memory storage or retrieval.

Limitations of the computational model, used as a basis to provide support for their theory, included its small sample size, lack of distributed representations among patterns, and excessively dense connections between neocortical areas (Alvarez & Squire, 1994). There have additionally been findings that retrograde amnesia is not always temporally graded (e.g. Schnider, Regard & Landis, 1994; Cermak & O'Connor, 1983), although this may be because of additional damage to neocortical structures in the anterior and lateral temporal lobes in these cases (Squire & Alvarez, 1995) which disrupted remote memory storage sites. Even so, this model does not account for the timeframe over which consolidation occurs (Kopelman & Bright, 2012). Some have suggested memories remain hippocampus-dependent for up to one week after initial learning (Frankland & Bontempi, 2005) whilst other findings suggest consolidation could extend for several years (Haist, Gore & Mao, 2001; Rempel-Clower, Zola-Morgan, Squire & Amaral, 1996).

1.1.3 Multiple Trace Theory

An alternative memory consolidation model to Alvarez and Squire's (1994) standard model is Nadal and Moscovitch's (1997) 'multiple trace theory'. They questioned whether all declarative memory was consolidated in the same way. Declarative memory consists of both episodic memory, i.e. knowledge about personal events, and semantic memory, i.e. knowledge of 'facts' about the world

(Tulving, 1972). Further distinctions can be made regarding autobiographical, or more personal, episodic and semantic memories. Nadal and Moscovitch proposed that different forms of declarative memory were differentially involved in consolidation between MTL and neocortical structures. This view was based on findings that the temporal gradient of retrograde amnesia was less extensive for autobiographical semantic memory and was absent for autobiographical episodic memory (Cermak & O'Connor, 1983; Damasio, Eslinger, Damasio & Van Hoesen, 1985; Tulving, Schacter, McLachlan & Moscovitch, 1988; Barr, Goldberg, Wasserstein & Novelly, 1990; Warrington & Duchen, 1992; McCarthy & Warrington, 1992; Kartsounis, Rudge & Stevens, 1995).

Additionally, considering the lack of quantification regarding the length of time taken to fully consolidate memories within the neocortex in the standard model and findings that the MTL was involved in retrieval of very remote retrograde memories (e.g. Rempel-Clower et al., 1996), Nadal and Moscovitch postulated that MTL structures were required for recovering even remote episodic memories. They suggested that the MTL was involved in both the storage and retrieval of episodic declarative memories throughout the lifetime, whilst general semantic information gradually became independent of the MTL.

The distinguishing features of multiple trace theory from the simple network model in its proposed stages of episodic memory consolidation include: (i) all reciprocal hippocampal-neocortical connections constitute the memory trace of an episode (information within the neocortex and spatial context within the hippocampus); (ii) re-activation of a memory trace results in re-encoding within the hippocampus and the creation of a new hippocampal trace; (iii) the process of hippocampal re-encoding results in a network of similar neocortical neurones, which share information about the initial episodic memory; (iv) factual information is extracted from the multiple, related, neocortical traces created and stored separately from the episodic memory, independent of the MTL; and (v) spatial and temporal contextual information of the episodic memory continues to depend on active involvement of the hippocampal region and other cortical structures. Thus, multiple trace theory assumes that episodic memories rely on multiple traces between the hippocampal region within the MTL and neocortex,

which continue to interact over time. The hippocampus remains vital for storage and retrieval of autobiographical contextual information. Newly acquired episodic memories have fewer traces, thus are more vulnerable to disruption following damage to the MTL; whilst older episodic memories (particularly those that have been retrieved frequently) have multiple traces, thus are more resilient to damage to part of the consolidation system.

Support for multiple trace theory has come from neuroimaging studies that have shown activation in MTL structures during retrieval of both recent and remote memories (e.g. Fink et al., 1996; Harand et al., 2012, Gilboa, Winocur, Grady, Hevenor & Moscovitch, 2004). However, Haist et al. (2001) found using functional magnetic resonance imaging (fMRI) that the hippocampus did not substantially contribute to the recollection of remote memories beyond a few years. Even so, they found that the entorhinal cortex had continued involvement in the memory consolidation process for up to 20 years. Therefore, this finding continues to support the premise of the multiple trace theory that memory traces do not become independent of MTL structures, as traces may be activated within a different system of the MTL. A meta-analysis of the functional neuroanatomy of autobiographical memory has additionally implicated both MTL and lateral temporal lobe regions in the retrieval of these memories, both for the recent and remote past (Svoboda, McKinnon & Levine, 2006).

However, Kopelman and Bright (2012) noted that adaptations made recently to the multiple trace theory (Winocur & Moscovitch, 2011) have given greater prominence to the process of 'transformation'. This process involves declarative memories transforming from hippocampal episodic or context-specific memories to para-hippocampal semantic versions of the memory. Nonetheless, this proposal bears similarities to the episodic-to-semantic shift theory of memory consolidation (Cermak, 1984): importantly, there is a lack of evidence that declarative memories become semanticised, and there is a danger of circularity in arguments for semanticisation of declarative memories (Kopelman & Bright, 2012).

1.2 Accelerated Long-Term Forgetting

1.2.1 Definition

'Classic' cases of amnesia typically have a neuropsychological profile of intact working memory systems with impaired anterograde episodic memory within seconds or minutes after information acquisition (Mayes et al., 2003; O'Connor, Sieggreen, Ahern, Schomer & Mesulam, 1997). However, a phenomenon has also been described whereby newly acquired episodic information is adequately retained over brief delays (i.e. minutes to hours), but then forgotten at an abnormally fast rate over longer delays (i.e. days to weeks). Recently, the phenomenon has been termed interchangeably as either 'long term amnesia' (Kapur et al., 1996, 1997) or 'accelerated long-term forgetting' (Blake, Wroe, Breen & McCarthy, 2000). For the purpose of this report, the latter term will be used. It is also worth noting that accelerated long-term forgetting may also be present in those whose initial performance on standard memory tests is already impaired (Baddeley, Rawlings & Hayes, 2013; Kopelman & Stanhope, 1997; Green & Kopelman, 2002).

1.2.2 Studies of Forgetting

Long-term forgetting was first investigated in people with severe memory impairment, often with discrete brain lesions in the temporal lobe or diencephalon. These lesion studies tended to investigate the differential effect of diencephalic damage versus MTL damage on long-term forgetting (e.g. Kopelman, 1985; Huppert & Piercy, 1979; Parkin & Leng, 1988; McKee & Squire, 1992). Initial interest in this topic arose from the study of HM, who had undergone bilateral ablation of the MTL cortex, in comparison to patients with Korsakoff's disease, with diencephalic lesions, and healthy controls (Huppert & Piercy, 1979). Conclusions from this study suggested HM exhibited accelerated long-term forgetting of a visual picture recognition task after matching performance between-groups at 10-minute delay. However, subsequent research showed variability in HM's forgetting rate when different methods of recognition retrieval were used (Freed & Corkin, 1988; Freed, Corkin & Cohen, 1987). This highlights the importance of method of retrieval used in the study of forgetting and the limitations of conclusions drawn from single case studies. A later group study

comparing these two lesion groups did not find evidence of accelerated long-term forgetting in the MTL group (McKee & Squire, 1992) nor did a study comparing patients with Korskoff's versus Alzheimer's disease, which is associated with hippocampal pathology (Kopelman, 1985). These findings further suggested that evidence of accelerated long-term forgetting was often only found when initial learning had not been sufficiently matched. They argued, therefore, that any apparently abnormal rate of forgetting was generally related to a deficit in acquisition as opposed to retention.

Later research, still comparing patients with diencephalic versus MTL lesions, used broader materials and methods to assess memory retrieval (Kopelman & Stanhope, 1997; Green & Kopelman, 2002; Isaac & Mayes, 1999a, 1999b). After matching short-term memory performance (i.e. 20- to 30-second), these studies found evidence for a retention deficit over medium-term delays (up to about 30-minutes) but only when using free recall as the method of retrieval. They suggested that these patient groups demonstrated primarily a difficulty in acquisition of new information but that they may additionally exhibit a subtler deficit in early retention that was only evident on free recall testing.

Long-term forgetting has also been investigated in people undergoing electro-convulsive therapy (ECT; Lewis & Kopelman, 1998; Squire, 1981). These studies modelled their procedure on that of Huppert and Piercy (1978, 1979) and found evidence of accelerated long-term forgetting after matching for short-term memory performance. This finding suggested the presence of accelerated long-term forgetting could be an effect of convulsions disrupting memory consolidation. This has, therefore, led to the study of this phenomenon in people with epilepsy.

Long-term forgetting has only relatively recently begun to be investigated in people with epilepsy, including those with generalised epilepsy, TLE and a sub-type of this, transient epileptic amnesia. As people with epilepsy do not tend to present with 'classic' amnesia and often do not exhibit detectable deficits in initial acquisition of material (Butler & Zeman, 2008b; Butler, Muhlert & Zeman, 2010), the potential existence of accelerated long-term forgetting in this population presents an interesting paradigm to elucidate if, when, and how long-term

forgetting occurs. Long-term forgetting in the context of epilepsy is discussed in greater detail below and forms the focus of the current study.

It is also worth noting that there may be an ageing effect regarding long-term forgetting, with evidence that healthy older adults exhibit accelerated long-term forgetting that cannot be accounted for by deficits in acquisition (Huppert & Kopelman, 1989; Mary, Schreiner & Peigneux, 2013; Manes, Serrano, Calcagno, Cardozo & Hodges, 2008).

1.2.3 Theoretical Implications

One approach to the study of memory consolidation has relied on cases and group studies investigating retrograde amnesia, which are difficult to control or manipulate experimentally (Butler et al., 2010). In addition, matching remote and recent memories for personal significance and vividness is very difficult (Addis, Moscovitch, Crawley & McAndrews, 2004). Long-term forgetting offers an alternative approach for the exploration of the systems involved in memory consolidation that can be investigated in an anterograde fashion and therefore be experimentally controlled. The phenomenon of accelerated long-term forgetting challenges the notion that once information has been successfully encoded into long-term memory, the information is relatively robust to forgetting. Contrastingly, it suggests there is a disruption to secondary long-term consolidation processes (Narayanan et al., 2012). Although the exact mechanisms involved in the disruption to secondary consolidation processes are currently unknown, the study of accelerated long-term forgetting could provide insight into the cognitive processes occurring and provide evidence to prove or disprove different theoretical models of memory consolidation. Investigation into the nature of which declarative memories are implicated, the structural systems involved, and other clinical variables relevant to long-term forgetting may all provide insight into how autobiographical declarative memories are consolidated into, and retrieved from, a long-term store (Butler et al., 2010; Mayes et al., 2003).

1.3 Epilepsy

1.3.1 Definition

An epileptic seizure is defined as "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" (Fisher et al., 2005, p. 471). Epilepsy is the overarching term for a variety of brain disorders of multiple aetiologies characterised by the occurrence of at least one epileptic seizure, an increased predisposition for future seizures due to an enduring epileptogenic abnormality in the brain, and associated neurobiological, cognitive, psychological, and social disturbances (Fisher et al., 2005).

1.3.2 Seizure Classification

Although there are many methods used to classify epileptic seizures, they have traditionally been classified based on seizure semiology, i.e. the clinical manifestations observed during the seizure, and the electroencephalographic (EEG) features of the seizure (Commission on Classification and Terminology of the International League Against Epilepsy [ILAE], 1981). Seizure classification according to this system is described further below.

1.3.2.1 Partial or Focal Seizures

Focal epilepsies are characterised by seizures originating in a restricted area of the cerebral cortex. They can be categorised into three broad types: (i) simple partial seizures where consciousness is not impaired but clinical signs include motor, somatosensory, autonomic, and/or psychic symptoms; (ii) complex partial seizures where there is an impairment of consciousness (either at seizure onset or following a simple partial seizure) and possible automatisms; and (iii) partial seizures with secondary generalised seizures, which may be tonic-clonic, tonic or clonic. Within this category, 'auras' are classified as simple partial seizures that can act as a signal for the onset of a complex partial seizure or occur in isolation.

1.3.2.2 Generalised Seizures

Generalised epilepsies include tonic, clonic, tonic-clonic, myoclonic, and absence seizures. They signify abnormal discharges of cerebral neurones involving large portions of the cortex bilaterally from seizure onset to cessation. Generalised seizures can either involve a large area of the cortex at onset or, as described

above, be secondary to a focal-onset partial seizure. Generalised seizures may be convulsive or non-convulsive and vary greatly with regard to severity.

1.3.2.3 Unclassified Epileptic Seizures

These are any seizures that cannot be categorised into the above groups.

1.3.3 Epidemiology

Epilepsy is one of the most common neurological disorders (Lee, 2010). The incidence of developing epilepsy is estimated to affect approximately 50 people per 100,000 per year in industrialised countries (Sander, 2003). 1.9 million adults aged 20-64 years are estimated to have epilepsy in Europe (Forsgren, Beghi, Oun & Sillanpää, 2005). Focal seizures are the most common form of epilepsy experienced amongst adults, accounting for approximately 55% to 83% of people with epilepsy (Annegers, 1996; Hauser & Kurland, 1975; Forsgren, 1992). However, epidemiological studies have been limited by their sampling, with a lack of population-based studies, a focus on prevalence of epilepsy in children, and bias towards those with more severe forms of epilepsy (Weibe, 2000).

1.3.4 Temporal Lobe Epilepsy

The Commission on Classification and Terminology of the ILAE (1989) classifies focal epilepsies according to the topographical origin of the seizure. Thus, focal epilepsies include, for example: TLE; frontal lobe epilepsy; parietal lobe epilepsy; and occipital lobe epilepsy. As TLE is the focus of this paper, this form of focal epilepsy will be described further in the following section.

The ILAE Commission (1989) characterises TLE by the presence of simple partial, complex partial, and/or secondary generalised seizures. Seizures may occur in either clusters at intervals or randomly and seizure focus may be either unilateral or bilateral in the temporal lobes as observed on EEG. Seizure focus may either be limbic or neocortical (Engel, 2001). Diagnosis is often made on the basis of a brain MRI scan (Antel et al., 2002; Duncan, 2001; Cendes, 2000; Li et al., 2000), EEG activity (Malow, Selwa, Ross & Aldrich, 1999; Pataraia et al., 1998; Cascino et al., 1996), and clinical ictal and postictal manifestations of seizure semiology.

Ictal clinical manifestations often include simple partial seizures characterised by sensory phenomena such as olfactory, auditory and epigastric sensations (also known as 'auras'), and complex partial seizures associated with automatisms, motor manifestations, and amnesia. Secondary generalised seizures are less common, and one-tenth of people with TLE will never experience a generalised seizure (Panayiotopoulos, 2005).

Postictal symptoms are common, and their clinical manifestation may implicate the lateralisation of the seizure's origin. Symptoms include fatigue, drowsiness, headache, aphasia, poor concentration, automatic behaviour, and confusion, often with the person exhibiting loss of memory of the symptoms. Aphasia and disorientation may suggest seizure focus in the language dominant hemisphere (Williamson et al., 1998; Dantas et al., 1998) whilst well-formed speech and rapid recovery may implicate the non-dominant hemisphere (Fakhoury, Abou-Khalil & Peguero, 1994).

1.3.4.1 Epidemiology and Aetiology

TLE is thought to comprise 30% to 35% of all epilepsies (Hauser, 1997; Crawford, 2000; Weibe, 2000) and it is the most common form of focal epilepsies (Manford, Hart, Sander & Shorvon, 1992; Sveinbjörnsdottir & Duncan, 1993; Engel & Shewmon, 1993). However, its true prevalence in the population remains unknown due to sampling and classification inconsistencies (Manford et al., 1992; Oka, Ishida, Ohtsuka & Ohtahara, 1995; Juul-Jensen & Foldspang, 1983).

People with TLE all have a seizure focus that originates within the temporal lobe but the aetiology of their epilepsy can be heterogeneous. Aetiologies of epilepsy are often defined as idiopathic, cryptogenic, or symptomatic (Shorvon, 2011; Lee, 2010). Idiopathic TLE refers to cases when no known cause is identified but the presence of seizures is assumed to have a genetic origin. Cryptogenic TLE refers to when the aetiology of epilepsy remains unknown and is thought to be due to acquired injury.

Symptomatic TLE refers to when a documented lesion is thought to be causally related to the presence of seizures within the temporal lobe (Shorvon, 2011; Lee,

2010). These lesions can be either within the mesial temporal lobe or within the lateral temporal lobe in the neocortex (Panayiotopoulos, 2005). Mesial TLE, with predominantly hippocampal sclerosis, is much more common than lateral TLE (where pathology is associated with extra-mesiotemporal sclerosis), accounting for two thirds of symptomatic cases of TLE (Engel et al., 2003). The origin of the pathology within temporal lobe structures is diverse and can include infections (particularly in infancy), tumours, cerebrovascular disorders, malformation of cortical development, trauma and other injuries (Mathern, Babb, Pretorius, Melendez & Levesque, 1995).

1.3.4.2 Prognosis and Treatment

The prognosis and response to treatment of TLE largely depends on its aetiology. Treatment of TLE often comprises anti-epileptic medication and/or neurosurgical excision of the epileptogenic region (Engel et al., 2003). Anti-epileptic medication includes both 'older' drugs traditionally used to control seizures, such as carabamazepine, phenytoin, phenobarbitone, clobazam, and valproate and 'newer' drugs such as oxcarbazepine, levetiracetam, lamotrigine, topiramate, zonisamide, tiagabine, and gabapentin (Panayiotopoulos, 2005). Neurosurgical treatment is considered in cases with refractory seizures despite anti-epileptic drug (AED) treatment with negative medical and psychosocial consequences (Lee, 2010).

1.3.4.3 Neuropsychological Profile

Variables associated with having epilepsy such as: (i) younger age of onset; (ii) history of generalised seizures; (iii) higher levels of antiepileptic drugs; (iv) frequent seizures; and (v) focal brain lesions have been shown to have negative cognitive effects in domains such as intelligence, attention, memory, executive functions, and visuo-motor speed (Lee, 2010). There is some evidence that people with TLE have cognitive impairments in the above domains with material-specific effects between left- and right-hemisphere seizure origin (Hermann, Seidenberg, Schoenfeld & Davies, 1997; Oyegbile et al., 2004). However, there does appear to be variability in this population in that not all patients with TLE exhibit cognitive impairment (e.g. Jokeit & Ebner, 1999). Additionally, much of the literature on accelerated long-term forgetting has documented comparable performance between participants with TLE and controls on standardised intelligence and

memory measures (Fitzgerald, Mohamed, Ricci, Thayer & Miller, 2013a; Witt, Glöckner & Helmstaedter, 2012).

1.3.4.4 Transient Epileptic Amnesia (TEA)

TEA has been posited as a distinctive sub-type of TLE whereby epileptic activity is associated with episodes of transient amnesia without impairment to other cognitive functions (Zeman, Boniface & Hodges, 1998). In a case review Zeman et al. (1998) documented that people with TEA typically had epilepsy of heterogeneous aetiologies and late onset of epilepsy, generally above the age of 40. They also noted that amnesic episodes tended to be brief and often occurred on waking. Often people with TEA also complain of 'gaps' in autobiographical and remote memory (Kopelman, Panayiotopoulos & Lewis, 1994; Kapur, 1990, 1993; Milton et al., 2010).

1.4 Accelerated Long-Term Forgetting in TLE

1.4.1 Overview

Accelerated long-term forgetting in epilepsy has been studied most extensively in people with TLE (Butler & Zeman, 2008b; Butler et al., 2010; Fitzgerald et al., 2013a). People with TLE frequently complain of memory problems (e.g. Butler et al., 2007; Fitzgerald et al., 2013a), yet a significant minority perform within 'normal' ranges on conventional measures of anterograde memory (Witt et al., 2012). Emerging literature has posited that the reason for this discrepancy may be due to a disruption of long-term memory consolidation over days, weeks, months, or years (Mayes et al., 2003; Fitzgerald et al., 2013a; Butler et al., 2010), thus suggesting that people with TLE may experience accelerated long-term forgetting. However, it is also worth noting that some people with TLE also exhibit memory deficits even at short recall delays, i.e. within 30 minutes (Witt et al., 2012; Bell, Fine, Dow, Seidenberg & Hermann, 2005; Giovagnoli, Casazza & Avanzini, 1995; Helmstaedter, Hauff & Elger, 1998). This means that some people with TLE may exhibit deficits in the initial learning and acquisition of anterograde declarative memory, and may also exhibit accelerated long-term forgetting during secondary consolidation processes (Helmstaedter et al., 1998; Mameniskiene et al., 2006; Bengner et al., 2006). However, to demonstrate differences at longer-term delays careful control for possible initial differences is important.

Table 1 describes the single case (N = 13) and group studies (N = 23) that have investigated long-term forgetting in epilepsy. Group studies that re-analysed previously conducted research were not included (i.e. Butler et al., 2009; Butler et al., 2013; Hoefeijzers, Dewar, Della Sala, Zeman & Butler, 2013) as they used the same group sample as Butler et al. (2007). Of all these studies, there have only been four published studies that have not found any evidence of accelerated forgetting (at any delay) in the TLE population (Bell, 2006; Bell et al., 2005; Djordjevic et al., 2011; Giovagnoli et al., 1995). Two have found evidence of accelerated forgetting over a medium-term delay, i.e. within an hour (McGibbon & Jansari, 2013; Kemp et al., 2012). Despite these majority findings implicating the presence of accelerated long-term forgetting, the studies investigating this phenomenon described above highlight the need for methodological rigour in these investigations: very few have robust methodology. Materials used to measure long-term forgetting and other methodological limitations in many of the studies listed in Table 1 may account for some, if not all, of the differences found and will be discussed further below. Before these are considered, the potential clinical importance of this phenomenon and possible pathophysiological aetiologies for accelerated long-term forgetting are reviewed.

1.4.2 Clinical Importance

Standardised anterograde memory tests are widely available, and well established, in clinical settings to measure memory deficits. However, these tests have traditionally revolved around detecting deficits in memory acquisition based on Atkinson and Shiffrin's (1968) distinction between 'short-term' and 'long-term' memory, whereby it is assumed memories are successfully consolidated in long-term memory within a short space of time, typically 30 minutes (Baddeley et al., 2013; Parkin, 1993). For example, the delay periods on widely used, standardised, memory measures (Wechsler, 1997; Baddeley, Emslie & Nimmo-Smith, 1994; Coughlan & Hollows, 1985) do not exceed 35 minutes. However, memories may be consolidated, but then be liable to disruption over a longer period of time, depending on how long consolidation processes last (e.g. O'Connor et al., 1997; Blake et al., 2000). This suggests that: (i) significant memory deficits affecting peoples' everyday functioning may not be currently assessed adequately clinically;

and (ii) standardised measures of anterograde memory may sometimes be insensitive to detect disruption to secondary memory consolidation processes due to their reliance on recall after medium-term delays. It is possible that standardised memory tests may also be insensitive to detect mild deficits in early consolidation processes within 30 minutes (Butler & Zeman, 2008b).

In addition, there are therapeutic implications for possible interventions if a patient shows accelerated long-term forgetting. Some strategies to manage epilepsy, such as anti-epileptic medication and epilepsy surgery have been suggested to ameliorate the effects of accelerated long-term forgetting (O'Connor et al., 1997; Evans, Elliott, Reynders & Isaac, 2014; Gallassi et al., 2011). For others where this is not an option, the use of memory strategies (Jansari et al., 2010) may also aid to improve forgetting rates, although these interventions are by no means well-established or of proven effectiveness.

Table 1: Summary of Case and Group Studies Investigating Long-Term Forgetting in Epilepsy*

Authors (year)	Initials / N Pts v. Con.	Patient age mean (SD)	Seizures	Seizure Laterality	Memory impairment at 30m?	ALF tests	Delay Trials	First delay AF found	Methodological Criteria					
									MC	V/ NV	ILM	m LTD	No C/F	No Rep.
CASE STUDIES														
Kapur et al. (1996)	SP	50	GTC	L	No	LM (stories) recall (+); LM (stories) recog (+); VR recall (+); VR recog (+); Pattern-colour PAL recog (-); Visual PAL recall (-); Visual PAL recog (-)	30m, 6w	6w	×	✓	ND	×	×	×
Kapur et al. (1997)	PA	62	TLE (CPS)	L	No	LM (stories) recall (+); LM (stories) recog (+); VR recall (+); VR recog (-)	Imm, 30m, 6w	6w	✓	✓	✓	×	×	×
O'Connor et al. (1997)	JT	42	TLE (CPS)	Bilat	No	Word list recall (+)	2h, 24h, 48h, 72h, 1w	24h	×	×	✓	✓	×	×
Lucchelli and Spinnler (1998)	GB	65	TLE (CPS)	L	Yes (verbal, mild)	Babock (stories) recall (+); RCFT recall (-)	Imm, 10m, 60m, 24h, 7d, 41d	7d	×	✓	×	✓	×	×
Holdstock et al. (2002); Mayes et al. (2003)	JL	46	TLE (CPS)	Bilat	No	Word-definition pairs recog (+); Story recall (+); Story recog (+); RCFT constructed recog task (-); Word recog (+); Face recog (+)	(2002) Imm, 30m, 24h, 4w	(2002) 4w	✓	✓	×	✓	×	✓
							(2003) 20s, 30m, 3w	(2003) 3w	✓	✓	×	✓	×	✓
Cronel-Olayon et al. (2006)	JE	18	TLE (CPS)	L	Yes (mild)	RAVLT (+), story (+); Verbal PAL (+); Rey's 15 drawings (+); RCFT recall (+)	Imm, 60m, 7d, 29d	7d	×	✓	×	✓	✓	×
Manning et al. (2006)	JR	54	CPS -> GTC	L	No			30h						
Butler and Zeman (2008a)	NR	54	TEA	L	No	15 item word list (+); 7-designs recall (+)	Imm, 30m, 7d, 3w	7d	×	✓	✓	✓	×	×
Jansari et al. (2010); McGibbon and Jansari (2013)	RY	63	TEA	R	No	Stories non repeated (+); Stories repeated (-); Word pair non repeated cued recall (+); Word pair repeated cued recall (-)	(2010) 30m, 24h, 7d, 2w, 4w	(2010) 24h	✓	×	ND	✓	×	✓
							(2013) 5m, 30m, 55m, 4h, 24h	(2013) 55m	✓	×	✓	✓	✓	✓
Gallassi et al. (2011)	MT	58	TLE (CPS -> GTC)	L	No	RAVLT (+); RCFT (+); Babock story (+)	30m, 7d	7d	×	✓	ND	×	×	×
Kemp et al. (2012)	SK	37	TLE (CPS)	Bilat	Yes (verbal and visual)	Story 1 recall (+); Story 2 recog (-); Family pictures (+); Word list recall (-)	Imm, 20m, 4d, 11d, 30d	20m	✓	✓	✓	✓	✓	×
	EB	73	TEA	ND	No	Story 1 (-); Story 2 (-); Family pictures (-)								
GROUP STUDIES														
Martin et al. (1991)	21/21	31 (7.5)	TLE	13 L; 8 R	No	Word list SRT (+)	30m, 24h	24h	×	×	✓	×	✓	×
Bergin et al. (1995)	48	Sz 26.5 (ND) no Sz 31 (ND)	7 SPS; 19 CPS; 3 CPS -> GTC; 1 NS; 18 no Sz (maj. TLE)	ND	No	AMIPB Story recall (-), list learning (-), figure recall (-); Face recog (-)	Imm, 30m, 48h	N/A	✓	✓	×	×	✓	×
Giovagnoli et al. (1995)	24/25	38 (11.6)	TLE	12 L; 12 R	No R; Yes L	Design SRT (-)	Imm, 1h, 24h, 3d, 6d, 13d	N/A	×	×	×	✓	✓	×
Helmstaedter et al. (1998)	55/21	26.9 (ND)	TLE	28 L; 27 R	Yes	Word list recall (+); Design recall (+)	Imm, 30m, 7d	7d	×	✓	×	×	✓	×
Blake et al. (2000)	21/16	33.76 (9.7)	14 TLE; 7 other	11 L; 10 R	No	Story recall (+), Story recog (+)	Imm, 30m, 8w	8w	✓	×	✓	×	×	×

* Table adapted and amended from Butler et al. (2010) and Fitzgerald et al. (2013a) with the addition of delay trials and methodological criteria column

Authors (year)	Initials / N Pts v. Con.	Patient age mean (SD)	Seizures	Seizure Laterality	Memory impairment at 30m?	ALF tests	Delay Trials	First delay AF found	Methodological Criteria					
									MC	V/ NV	ILM	m LTD	No C/F	No Rep.
Jokeit et al., (2001)	10	36 (14.6)	TLE	4 L; 6 R	ND	Word list (+; L TLE)	Imm, 30m, 24h	24h	×	×	ND	×	ND	×
Bell et al. (2005)	42/49	L 34 (13.0); R 40 (9.8)	TLE	22 L; 20 R	Yes	Word list SRT recall (-); Design SRT recall (-)	Imm, 30m, 24h	N/A	×	✓	×	×	✓	×
Manes et al. (2005)	7/7	57 (8.1)	TEA	6 bilat; 1 EEG normal	No	Stories recall (+), Stories recog (+); VR recall (-), VR recog (-)	Imm, 30m, 6w	6w	✓	✓	×	×	×	×
Bell (2006)	25/25	39 (10)	TLE	11 L; 6 R; 2 bilat	Yes	Stories recall (-), Stories recog (-)	Imm, 30m, 2w	N/A	×	×	×	×	✓	×
Bengner et al. (2006)	56/12	39.2 (11.8)	44 TLE; 12 IGE	20 L: 7 MRI (+), 13 MRI (-) 24 R: 13 MRI (+), 11 MRI (-)	Yes R MRI (+) only	Face recog (+)	Imm, 24h	24h	✓	×	×	×	✓	×
Mameniskiene et al. (2006)	70/59	33 (9.5)	TLE	ND	Yes	Word list recall (+), Stories recall (+); RCFT recall (+);	Imm, 30m, 4w	4w	×	✓	×	×	✓	×
Butler et al. (2007)	24/24	68 (8.7)	TEA	8 L; 6 R; 4 bilat; 16 slow wave; 15 EEG n	No	Word list recall (+); Designs recall (+)	Imm, 30m, 7d, 3w	7d	✓	✓	✓	✓	×	×
Davidson et al. (2007)	21/21	11.5 (ND)	IGE	N/A	No	CMS Stories recall (+), recog (-); CMS Dot Locations recall (-), recog (-)	30m, 7d	7d	✓	✓	✓	×	✓	×
Mulhert et al. (2010)	11/11	68.9 (9.9)	TEA	ND	No	Word list (WL, +); SenseCam recall (SC, +)	30s (WL), 4h (SC), 24h, 7d, 3w	24h	✓	✓	×	✓	✓	×
Deak et al. (2011)	6/9	44 (ND)	TLE	ND	No	SRT (+); Finger motor tapping sequence task (-)	Imm, 30m, 12h	12h	✓	×	✓	×	×	×
Djordjevic et al. (2011)	90/19	L 33.5 (ND); R 36.8 (ND)	TLE	46 L; 44 R	No R; Yes L	Story recall (-)	Imm, 30m or 24h	N/A	×	×	ND	×	ND	×
Mulhert et al. (2011)	28/15	TLE 46.4 (11); IGE 31.6 (14.6)	14 TLE; 14 IGE	2 L; 2 R; 2 bilat; 8 ND	No	Visual scenes recall (+), recog (-); Spatial discrimination (-); Descriptive recall (+) Story recall (-), Story recog (+)	40s, 30m, 3w	3w	✓	✓	×	×	✓	✓
Tramoni et al. (2011)	5/15	42.6 (9.3)	4 TLE; 1 TEA	1 L; 2 R; 3 bilat	No	Stories (+); Routes (+); Chain of episodes (+); List of facts (-); Single-item (-)	1h, 6w	6w	✓	✓	ND	×	×	×
Gascoigne et al. (2012)	20/41	10.76 (2.47)	IGE	N/A	No	Word list (+)	2m. 30m, 7d	7d	×	×	✓	×	×	×
Narayanan et al. (2012)	14/17	33.5 (10.13)	TLE	8 L; 6 R	No	RAVLT (+); RCFT (-); Labyrinth maze (-); Autobiographical event test (+)	30m, 4w	4w	✓	✓	×	×	✓	×
Wilkinson et al. (2012)	27/22	L 34.8 (10.1); R 38.7 (8.1)	TLE	15 L; 12 R	No	Story recall (+); Figure recall (+)	Imm, 1h, 6w	6w	✓	✓	✓	×	✓	×
Fitzgerald et al. (2013b)	35/15	F 41.80 (14.60) G 32.60 (14.54) n 36.89 (10.47)	10 F: 9 FT, 1 Occ; 5 G; 18 n	F: 4 L FT; 2 R FT; 3 bilat FT; 1 bilat Occ	No	Word list recall (+, F); Design list recall (+, G)	30m, 24h, 4d	24h	✓	✓	ND	✓	×	×
Evans et al. (2014)	7/25	39.71 (15.77)	TLE	3 L; 4 R	No	Visual scenes free recall (-), spatial recall (+), descriptive recall (-), recog (-); Story recall (+), recog (+); Repeated story recall (-), recog (+)	24 or 45s, 30m, 1w	1w	✓	✓	×	×	✓	✓

Index: ALF = accelerated long-term forgetting, AF = accelerated forgetting, AMIPB = The Adult Memory and Information Processing Battery, Bilat = bilateral, CMS = Children's Memory Scale, Con. = controls, CPS = complex partial seizure, d = days, F = focal, FT = fronto-temporal, G = generalised, GTC = generalised tonic clonic, h = hours, IGE = idiopathic generalised epilepsy, IML = initial matched learning (on all measures), Imm = immediate, L = left, LM = Logical Memory, m = minutes, m LTD = multiple long-term delays, maj. = majority, MC = matched controls, MRI = magnetic resonance imaging, NS = nocturnal seizure, n = normal, ND = not disclosed, no C/F = no ceiling / floor effects, Occ = occipital, R = right, PAL = paired associate learning, Pts. = patients, RAVLT = Rey Auditory Verbal Learning Test, RCFT = Rey Complex Figure Test, recog = recognition, s = seconds, SD = standard deviation, SPS = simple partial seizure, SRT = serial reaction time, Sz = seizures, TLE = temporal lobe epilepsy, TEA = transient epileptic amnesia, V/NV = verbal / non-verbal, VR = Visual Reproduction, w = weeks, (+) = AF evidenced, (-) = no AF

1.4.3 Pathophysiology

Several mechanisms have been hypothesised to be involved in the causation of accelerated long-term forgetting in epilepsy (Butler & Zeman, 2008b; Butler et al., 2010). These include: (i) the presence of clinical and subclinical seizures; (ii) structural pathology; (iii) adverse effects of anti-epileptic medication; and (iv) psychological mechanisms.

1.4.3.1 Clinical and Subclinical Seizure Activity

Although inducing convulsions through ECT has been postulated to disrupt long-term memory consolidation (Lewis & Kopelman, 1998), the question of whether clinical or subclinical levels of seizure activity within the temporal lobe is sufficient for accelerated long-term forgetting to occur has not been comprehensively answered (Kopelman, 2000; Kopelman, 2002). In groups with TLE, both manifest seizures and subclinical epileptiform activity, measured using EEG, have been found to be positively correlated with long-term forgetting rates (Mameniskiene et al., 2006; Wilkinson et al., 2012). However, this correlation has not consistently been found in the literature and accelerated long-term forgetting rates are not always associated with seizure activity during the experimental delay period (Blake et al., 2000; Mulhert et al., 2011)

Jokeit, Daamen, Zang, Janszky and Ebner (2001) used videotelemetry and found that patients with a left temporal lobe epileptiform focus exhibited poorer recall of verbal material after 24 hours, compared to patients with epileptiform focus elsewhere, supporting the hypothesis that temporal lobe seizures disrupt memory consolidation processes. Additionally, Evans et al. (2014) posited that improvements they found in accelerated long-term forgetting rates following epilepsy surgery were related to greater control of seizure activity following surgery. Even so, this relationship between focal seizure activity and greater long-term forgetting has not consistently been found (Bergin, Thompson, Fish & Shorvon, 1995; Fitzgerald, Thayer, Mohamed & Miller, 2013b). In these studies, accelerated long-term forgetting has either been found not to be associated with any epileptiform activity, focal or generalised (Bergin et al., 1995), or only in patients with generalised seizures (Fitzgerald et al., 2013b). However, neither of

these studies' focal seizure groups consisted exclusively of patients with TLE; therefore may be limited in their applicability to the question of whether epileptiform activity in the MTL disrupts memory consolidation processes, thereby leading to accelerated long-term forgetting.

Even so, even when seizures have been completely controlled for over a year, accelerated long-term forgetting of declarative memories has still been demonstrated in cases of TLE and TEA (Butler et al., 2007; Tramoni et al., 2011). Controlling seizures with the use of anti-epileptic medication has also been found not to improve the accelerated rate of long-term forgetting of verbal information in a case with TEA (Jansari et al., 2010), although this finding is variable (e.g. O'Connor et al., 1997). Additionally, the suggestion that seizure activity disrupts memory consolidation, thus leading to accelerated long-term forgetting, does not explain why such activity does not always interrupt initial memory consolidation at short delays (Jansari et al., 2010).

This inconsistent association between accelerated forgetting and manifest seizure activity has led some to suggest it is the subclinical activity that is most instrumental in disrupting consolidation processes (Butler & Zeman, 2008b). An interesting link between the possible contribution of subclinical epileptiform activity and sleep is particularly noteworthy. Evidence suggests that sleep is important in the consolidation of declarative memories (e.g. Drosopoulos, Schulze, Fischer & Born, 2007; Ellenbogen, Hulbert, Stickgold, Dinges & Thompson-Schill, 2006). Considering the relationship often seen in TEA between waking and transient amnesic episodes (Butler & Zeman, 2008a; 2008b), it is possible that nocturnal subclinical epileptiform activity is instrumental in disrupting memory consolidation processes. However, the association between epileptiform activity during nocturnal sleep and the presence of accelerated forgetting is weak in the published studies examining this question in epilepsy (Bengner et al., 2006; Deak, Stickgold, Pietras, Nelson & Bubrick, 2011; Fitzgerald et al., 2013b).

Considering the methodological difficulties controlling the timing, duration, and anatomical focus of seizures, which may all play an important role in the extent of disruption to memory consolidation processes (Butler et al., 2010), it is not

surprising such contradictory findings have been found in the literature. Although it has been suggested there may be some relationship between subclinical epileptiform activity and the disruption of secondary processes of memory consolidation (Butler & Zeman, 2008b), the exact contribution and processes involved in this disruption are currently unknown.

1.4.3.2 Structural Brain Pathology

The presence of MTL pathology in almost all the epilepsy case reports that have described accelerated long-term forgetting (with the exceptions of Lucchelli & Spinnler, 1998; and Jansari et al., 2010) has led some authors to suggest subtle damage to the MTL may play a role in accelerated long-term forgetting. Similarly, lesion studies investigating accelerated forgetting over shorter delays have implicated the MTL and diencephalic systems in the retention of freely recalled material (e.g. Kopelman & Stanhope, 1997; Green & Kopelman, 2002). Some have suggested subtle MTL pathology may simply represent a milder form of the amnesic syndrome that is typically associated with more severe damage to the MTL (Mayes et al., 2003). Considering that accelerated long-term forgetting has been documented in patients with aetiologies other than epilepsy, structural damage to this region may be implicated in the development of this phenomenon.

However, this suggestion does not account for why people with TLE often perform normally at standard testing intervals yet forget information more rapidly over longer-term delays. Additionally, the presence of MTL pathology and findings of accelerated long-term forgetting in TLE group studies have been more variable than in case reports, with only the minority of patients who demonstrated accelerated long-term forgetting also having concomitant structural pathology (Blake et al., 2000; Mamneniskiene et al., 2006; Manes, Graham, Zeman, de Luján Calcagno & Hodges, 2005; Butler et al., 2007). Of 113 patients in the studies reviewed by Butler et al. (2010) who demonstrated accelerated long-term forgetting, only 17 reported the presence of structural brain pathology on neuroimaging. In addition, Evans et al. (2014) found that some patients with TLE demonstrated an improved rate of forgetting following epilepsy surgery.

Even so, Mulhert et al. (2011) found that accelerated long-term forgetting of declarative memory measures between medium-term (30-minute) delay and long-term (three-week) delay was more frequently identified in patients with TLE who also had mesial temporal sclerosis. This suggests that structural pathology in the MTL may disrupt secondary memory consolidation processes. However, others have found that structural MTL damage is only implicated in the initial acquisition and retention of material over the medium-term delay, and not at long-term delay (e.g. Butler et al., 2009). Additionally, Wilkinson et al. (2012) found that in patients with TLE who had hippocampal sclerosis, lateralisation of hippocampal pathology was associated with a material-specific effect in declarative memory acquisition and initial retention over a medium-term (one-hour) delay, but not at long-term (six-week) delay. Patients with right hippocampal sclerosis displayed normal retention of verbal information at one-hour but accelerated long-term forgetting by six-weeks, whilst patients with left hippocampal sclerosis displayed impaired retention of this material at one-hour as well as accelerated long-term forgetting by six-weeks. This finding suggests that MTL damage may disrupt initial memory acquisition and retention of declarative memories, but is not influential in secondary consolidation processes. It may also explain why accelerated long-term forgetting can sometimes still be observed in patients who also have impaired memory performance at standard delay (e.g. Helmstaedter et al., 1998; Mameniskiene et al., 2006).

The presence of pathology within different structures of the MTL may differentially affect memory consolidation processes, with hippocampal abnormalities associated with disruption to initial memory retention and pathology in more diffuse lateral structures associated with disruption to secondary consolidation processes. However, current studies investigating the role of structural pathology in accelerated long-term forgetting are limited by insufficiently sensitive imaging methods to detect structural abnormalities (Butler et al., 2010). Studies utilising functional connectivity techniques, such as diffusion tensor imaging, have shown that in patients with TLE there is reduced functional connectivity within the hippocampal gyrus ipsilateral to seizure activity (Yogarajah et al., 2008), but studies are yet to investigate the relationship between long-term forgetting and possible functional changes in the MTL or more subtle structural changes.

1.4.3.3 Anti-Epileptic Medication

There is some evidence that AEDs have a negative impact on cognition, particularly reducing processing speed and attention capabilities (Motamedi & Meador, 2003). AEDs have also been found to negatively impact memory performance and early retention of verbal and visual material (Motamedi & Meador, 2004; Jokeit, Krämer & Ebner, 2005).

It has been suggested that it is unlikely AEDs are solely implicated in findings of accelerated long-term forgetting since patients tend to complain of memory problems prior to initiation of medication. Additionally, they usually report their memory to improve after initiation of medication and medication doses for patients with TEA, who most often complain of accelerated long-term forgetting, are typically low (Butler & Zeman, 2008b; Butler et al., 2010). Accelerated long-term forgetting has also been demonstrated in a case before they were commenced on anti-epileptic medication (Jansari et al., 2010) and medication has sometimes been shown to improve long-term forgetting rates (Midorikawa & Kawamura, 2007; O'Connor et al., 1997). Thus, the evidence currently does not implicate AEDs in findings of accelerated long-term forgetting.

1.4.3.4 Psychological Factors

Psychological factors, such as low mood and poor self-esteem, have been hypothesised to influence patients' with TLE perceptions of their memory performance (Elixhauser, Leidy, Meador, Means & William, 1999; Giovagnoli et al., 1995). Some have suggested the disparity between subjective reports of memory difficulties and intact performance on standard neuropsychological tests in patients with TLE can be explained by these factors (Corcoran & Thompson, 1992). However, recent accelerated long-term forgetting studies that have assessed mood have only found a relationship between subjective memory ratings and mood (Butler et al., 2009), and found no correlation between mood and accelerated long-term forgetting rates (Blake et al., 2000; Butler et al., 2007; Mameniskiene et al., 2006; Muhlert et al., 2011). This suggests that whilst low mood may influence subjective experience of poor memory it does not influence findings of accelerated forgetting. Additionally, this phenomenon has not been established in patients with depression who have not undergone ECT (Lewis & Kopelman, 1998).

Therefore, it is unlikely mood plays a causal factor in accelerated long-term forgetting in TLE.

1.5 Measurement of Long-Term Forgetting

The assessment of long-term forgetting faces a number of methodological challenges that has often resulted in contradictory findings in the literature and limited the efficacy of the conclusions drawn in some studies (Butler & Zeman, 2008b; Butler et al., 2010). These methodological challenges are discussed further in this section.

1.5.1 Groups

It is possible that the type of patient group selected to investigate long-term forgetting may result in different effect sizes (Butler & Zeman, 2008b). Studies investigating long-term forgetting in epilepsy use groups with TLE, TEA and/or more generalised forms of epilepsy. Although people with TEA more commonly self-report symptoms of accelerated forgetting to a greater extent than the broader population with TLE (Butler et al., 2007), this patient group is rare and the phenomenon has also been demonstrated in people with TLE (e.g. Mulhert et al., 2011; Wilkinson et al., 2012). Therefore, it is possible that examination of accelerated long-term forgetting in a sample with TEA may exaggerate the effect observed in the wider TLE population, whilst including those with more generalised epilepsy may lessen the effect.

Crucially, matching patient and control groups for cognitive and demographic variables is hugely important in any case-control study, to ensure that conclusions made have isolated the effect of the dependent variable, in this case long-term forgetting. Considering there is some evidence for an age effect in long-term forgetting this is particularly important (Mary et al., 2013; Baddeley et al., 2013; Huppert & Kopelman, 1989; Manes et al., 2008). However, many published studies examining this phenomenon have failed to match groups to cognitive variables, such as IQ (e.g. Martin et al., 1991; Helmstaedter et al., 1998; Bell, 2006; Bell et al., 2005; Kapur et al., 1996) making the conclusions drawn in these studies somewhat limited.

1.5.2 Materials

Study materials used to investigate long-term forgetting are likely to result in different findings, particularly when taking into account laterality of seizure focus (Butler et al., 2010).

1.5.2.1 Verbal Material

The choice of verbal material used may result in variable forgetting profiles, for instance context-rich (e.g. a story) and context-free (e.g. a word list) verbal material has been shown to have differential forgetting rates (Isaac & Mayes, 1999a; 1999b). Many studies have used standardised tests, such as the Wechsler Memory Scale – Revised (e.g. Tramoni et al., 2011) and the Rey Auditory Verbal Learning Test (e.g. Butler et al., 2007) with an added long-term delay whilst others have designed verbal material for the purpose of the study (e.g. Djordjevic et al., 2011; Evans et al., 2014). Even so, accelerated long-term forgetting has been demonstrated using both list learning and story tasks (e.g. Mulhert, Milton, Butler, Kapur & Zeman, 2010; Evans et al., 2014). Despite this, word list tasks have been shown to be less predictive of everyday memory complaints than story tasks (Sunderland, Harris & Baddeley, 1983) and have less ecological validity than story passages (Baddeley et al., 2013).

Some studies have shown that laterality of seizure focus is implicated in long-term forgetting, with left-sided seizure focus associated with accelerated long-term forgetting of verbal information (Blake et al., 2000; Wilkinson et al., 2012; Jokeit et al., 2001). However, lateralisation effects have not been found in all studies (e.g. Martin et al., 1991; Mulhert et al., 2011).

1.5.2.2 Non-Verbal Material

Non-verbal tasks used in the accelerated long-term forgetting literature range from abstract design recall tasks (e.g. Fitzgerald et al., 2013b), facial recognition (e.g. Bengner et al., 2006), to spatial tasks with varying levels of ecological validity (e.g. Tramoni et al., 2011; Narayanan et al., 2012). Similarly to verbal material, some have used standardised tests, such as the Rey-Osterreith Complex Figure (e.g. Wilkinson et al., 2012) with an added long-term delay. The heterogeneity of non-verbal tasks in the literature is likely to be related to the inconsistent findings

of a relationship between accelerated long-term forgetting and non-verbal material. For instance, Evans et al. (2014) found that spatial recall from visual scenes was associated with accelerated long-term forgetting whilst free recall of the visual scene was not. However, other studies have found inconsistent results even when using the same complex figure recall task (e.g. Mameniskiene et al., 2006; Narayanan et al., 2012). Many tasks that are traditionally classified as 'non-verbal' on the surface can also be verbalised, and thus they may not be a pure measure of non-verbal ability (Narayanan et al., 2012).

Laterality of seizure focus is less well established with regards to non-verbal material and long-term forgetting, which is likely reflective of the heterogeneous methods of measuring non-verbal material. Some studies have shown no laterality effect (e.g. Martin et al., 1991; Mulhert et al., 2011). However, there have been findings of a trend towards right-sided seizure focus associated with accelerated long-term forgetting of non-verbal information (Wilkinson et al., 2012; Narayanan et al., 2012), suggesting it is still important to clarify laterality of seizure focus in accelerated long-term forgetting studies.

1.5.3 Pragmatics of Forgetting Measurement

1.5.3.1 Initial Learning

Different studies investigating long-term forgetting have found differing levels of performance at initial learning, with some studies demonstrating that the patient group showed intact learning and retention at initial delays (e.g. Blake et al., 2000; Butler et al., 2007; Martin et al., 1991) whilst the patient group in others performing relatively worse than controls (e.g. Bell, 2006; Bell et al., 2005; Helmstaedter et al., 1998; Giovagnoli et al., 1995). In those studies where the groups were not well matched on initial learning, this difference may then account for differential long-term forgetting rates.

Butler and Zeman (2008b) have suggested a number of techniques to utilise when the patient group may show impaired initial learning performance, including: (i) to modulate exposure to study material between groups to ensure both groups reach the same level of initial learning (Huppert & Piercy, 1978, 1979); (ii) to match

individual patients and controls for learning on a case-by-case basis; or (iii) to examine the overall shape of the forgetting curve rather than attempt to match initial learning. However, this last method is not recommended due to possible scaling effects between high- and low- learners and lack of comprehensive understanding regarding how much initial learning interacts with forgetting over time (Loftus, 1985; Rubin & Wenzel, 1996).

Some possible concerns to note with the proposed methods to match initial learning include the possibility of patients over-learning material and exhibiting a ceiling effect, which has been evidenced in some studies of accelerated long-term forgetting (e.g. Blake et al., 2000; Butler et al., 2007). Performing at ceiling, whether in the patient or control group, can mask differences in later forgetting rates and so is important to avoid (Kopelman, 2000; Davidson, Dorris, O'Regan & Zuberi, 2007; Mulhert et al, 2011).

1.5.3.2 Time Frame

The length of time between testing intervals may result in different findings. Some studies have demonstrated forgetting rates are most pronounced in the first day after learning, with negligible forgetting following this (Mulhert et al., 2010; Martin et al., 1991; O'Connor et al., 1997). Other studies have found intact memory after one day (e.g. Holdstock et al., 2002; Lucchelli & Spinnler, 1998), with accelerated forgetting thereafter. There may be a neurological reason for differences in forgetting over delays of one day versus forgetting over longer delays, such as differing structural damage or functional connectivity along the hippocampal-neocortical axis (Holdstock et al., 2002), thus it is important to include this time point in studies of accelerated long-term forgetting. Further, some studies have not included a one-day measurement (e.g. Blake et al., 2000; Tramoni et al., 2011; Wilkinson et al., 2012), only measuring the first long-term delay up to eight weeks later. Considering that most forgetting may occur before this length of time, it is important to include multiple long-term delays to determine when accelerated forgetting first occurs.

Additionally, at very long-term delays (e.g. eight weeks) it is likely both patients and controls will perform at floor (as noted in Blake et al., 2000), which also masks

differences in forgetting rates. Therefore, in long-term forgetting studies it is important to choose multiple testing intervals that demonstrate the course of forgetting in which patient and control participants neither exhibit ceiling effects at initial learning nor floor effects at long-term delay.

1.5.3.3 Nature of Retrieval

Different studies investigating accelerated long-term forgetting have used free recall, cued recall and recognition of material to varying degrees. However, these methods of retrieval can result in differing findings (Kopelman & Stanhope, 1997; Green & Kopelman, 2002; Isaac & Mayes, 1999a). When differences have been found in forgetting rates between recall and recognition (e.g. Davidson et al., 2007; Martin et al., 1991), this has been used to suggest that accelerated long-term forgetting is due to a retrieval, rather than storage, problem. However, findings have not been consistent, with some studies demonstrating accelerated long-term forgetting even for recognition memory (Helmstaedter et al., 1998; Blake et al., 2000; Bell et al., 2005; Manes et al., 2005; Bell, 2006). The difference in performance between recall and recognition at long-term delays may be informative for understanding what consolidation processes are involved in the presence of accelerated long-term forgetting. The use of cued recall at long-term testing intervals may be particularly useful in investigations of this phenomenon as this approach allows greater control of retrieval than free recall and has greater sensitivity than recognition (Baddeley et al., 2013).

Most studies investigating accelerated long-term forgetting have repeated recall of the same material at each testing interval (Bergin et al., 1995; Helmstaedter et al., 1998; Blake et al., 2000; Jokeit et al., 2001; Bell et al., 2005; Manes et al., 2005; Bell, 2006; Mameniskiene et al., 2006; Butler et al., 2007; Mulhert et al., 2010; Mulhert et al., 2011; Tramoni et al., 2011; Narayanan et al., 2012, Fitzgerald et al., 2013b). However, repeated recall has been shown to encourage rehearsal of information and consequently disguise the natural course of forgetting (Roediger & Karpicke, 2006; Karpicke & Roediger, 2008). It is likely that repeated probing results in the material being re-encoded and acts as a new learning trial at each testing interval. In fact, Jansari et al. (2010) demonstrated in a case report of a patient with TLE that repeatedly recalled information resulted in comparable long-term forgetting

to controls compared to non-repeatedly recalled information, which the patient with TLE forgot at an accelerated rate to controls. This suggests that repeated recall could counteract the effect of accelerated long-term forgetting, either through strengthening the transfer of material from the MTL to the neocortex or by creating multiple memory traces.

Recently, studies have increasingly attempted to develop methods to minimize repeated recall with the use of multiple tests (e.g. Evans et al., 2014; Jansari et al., 2010). Baddeley et al. (2013) suggested that when designing studies investigating accelerated long-term forgetting to increase the amount of material learned initially, and subsequently test recall on different subsets of this material at each recall interval. This method has also been used in past long-term forgetting studies (Huppert & Piercy, 1978, 1979). However, establishing an appropriate balance of material to be learned initially is difficult, and may result in either a heavy initial load or unacceptably small sample of data at each time interval. Establishing parallel forms of material is also a challenging task and the studies in the literature that have attempted using multiple tests have not tended to demonstrate the equivalency of their multiple forms (e.g. Evans et al., 2014; Jansari et al., 2010). One study retrospectively showed that their parallel forms (to assess long-term forgetting pre- versus post-surgery) were not equivalent to each other, limiting the conclusions able to be drawn (Djordjevic et al., 2011).

1.5.3.4 Other Pragmatic Issues

The determination of which long-term delay interval is used to assess forgetting has often been decided based on pragmatic reasons in the literature, such as repeat clinic appointments (e.g. Blake et al., 2000). This has limited understanding of the time scale over which long-term forgetting occurs and increases the likelihood of performing at floor due to the long time between appointments. However, recently the use of telephone follow-up calls to assess recall of verbal material at long-term delays has been trialled with promising feasibility (e.g. Baddeley et al., 2013; Gascoigne et al., 2012; Kemp et al., 2012).

Studies have additionally varied in relation to whether participants are forewarned about the long-term testing intervals. Forewarning may increase the

probability of participants attempting to rehearse material between test sessions, which may confound results (Butler et al., 2010). However, the question of whether forewarning does increase the likelihood of rehearsal has not been comprehensively investigated and so whether there is a relationship between forewarning and rehearsal is not currently known. Even so, it is likely that if a participant did rehearse material this would affect their rate of forgetting.

1.5.4 Critique of the Current Literature

The measurement issues that are important to account for in long-term forgetting studies have been described above. However, very few studies have conducted methodologically robust studies through: (i) matching the groups of investigation on cognitive and demographic variables; (ii) using both verbal and non-verbal materials; (iii) matching each group's performance at initial learning; (iv) measuring long-term recall at multiple informative delays; (v) avoiding ceiling and floor effects in the data; and (vi) avoiding repeated testing of material (see Table 1).

With regards to the 14 case studies in the literature, most did not match the patient to controls for IQ (the exceptions being Holdstock et al., 2002; Jansari et al., 2010; Kapur et al., 1997; Kemp et al., 2012; Mayes et al., 2003; McGibbon & Jansari, 2013). Two only used verbal material (Holdstock et al., 2002; Jansari et al., 2010) whilst one only used visuo-spatial material (Lucchelli & Spinnler, 1998). Additionally, few matched for initial learning on all measures (Butler & Zeman, 2008a; Kapur et al., 1997; Kemp et al., 2012; McGibbon & Jansari et al., 2013; O'Connor et al., 1997) whilst some did not report initial learning performance (Kapur et al., 1996; Jansari et al., 2010; Gallasi et al., 2011). The majority exhibited ceiling and floor effects (the exceptions being Cronel-Ohayon et al., 2006; Kemp et al., 2012; McGibbon & Jansari, 2013). Most studies repeated recall of the same material at each testing interval (the exceptions being Holdstock et al., 2002; Mayes et al., 2003; Jansari et al., 2010; McGibbon & Jansari, 2013). Additionally, two only measured recall at two time points (Kapur et al., 1996; Gallassi et al., 2011).

With regards to the 23 group studies, nine studies did not match the patient and control groups for IQ (Bell, 2006; Bell et al., 2005; Djordjevic et al., 2011; Gascoigne et al., 2012; Giovagnoli et al., 1995; Helmstaedter et al., 1998; Jokeit et al., 2001; Mameniskiene et al., 2006; Martin et al., 1991). Nine only used verbal material (Bell, 2006; Blake et al., 2000; Butler et al., 2007; Deak et al., 2011; Djordjevic et al., 2011; Gascoigne et al., 2012; Jokeit et al., 2001; Martin et al., 1991; Mulhert et al., 2010) and two only used visuo-spatial material (Bengner et al., 2006; Giovagnoli et al., 1995). Most did not match all measures for initial learning performance and others did not report this (the exceptions being Blake et al. 2000; Butler et al., 2007; Davidson et al., 2007; Deak et al., 2011; Gascoigne et al., 2012; Martin et al., 1991; Wilkinson et al., 2012). Additionally, many exhibited ceiling or floor effects (Blake et al., 2000; Butler et al., 2007; Deak et al., 2011; Fitzgerald et al., 2013b; Gascoigne et al, 2012; Manes et al., 2005; Tramoni et al., 2011). Finally, most studies repeated recall of the same material at each testing interval (the exceptions being Evans et al., 2014; Mulhert et al., 2011). Additionally, five only measured recall at two time points (Martin et al., 1991; Bengner et al., 2006; Davidson et al., 2007; Tramoni et al., 2011; Narayanan et al., 2012). This comparison highlights the limitations of the literature currently and the need for greater methodological rigour when designing long-term forgetting studies in this population.

1.6 The Current Study

1.6.1 Study Rationale

In summary, the study of accelerated long-term forgetting provides an interesting approach with which to investigate memory consolidation processes. This phenomenon has most extensively been demonstrated in people with TLE and TEA; which, if robust, may suggest that pathophysiology associated with epilepsy originating within the temporal lobes may play a key role in the disruption to secondary memory consolidation processes. The exact processes occurring are currently unknown but research into this question has typically been methodologically flawed, although it should be acknowledged that this is a methodologically challenging research topic. Additionally, although recent research has begun to establish the feasibility of assessing long-term recall remotely, this has been limited. Thus, there is a need in the literature to develop

measures that are both sound in method and convenient in practice with which to assess long-term forgetting in the population with TLE. Accurate elucidation of whether, when and how forgetting occurs will have both important clinical and theoretical implications.

1.6.2 Aims

The current study aimed to investigate long-term forgetting in people with TLE on two measures, a verbal and a visuo-spatial memory task. These were developed for the purpose of the study with the aim of minimising the methodological difficulties described above. The feasibility of assessing long-term recall of visuo-spatial material remotely in a fashion similar to verbal material was also investigated.

Thus, the aims of the study were two-fold. In the first instance, it was aimed to develop a verbal and visuo-spatial task and that these measures met the following methodological criteria: (i) minimised repeated recall of the same material; (ii) avoided ceiling effects at the first recall delay; (iii) avoided floor effects at the last recall delay; and (iv) established how to match groups at initial learning. In the second instance, it was aimed to use these measures in a case-controlled study comparing participants with TLE to neurologically healthy control participants who were matched on demographic and cognitive variables, to investigate accelerated long-term forgetting.

1.6.3 Hypotheses

With respect to the case-control study, the main hypotheses were:

1. Participants with TLE will demonstrate accelerated forgetting on the story task after immediate learning.
    a. Some (e.g. Kopelman & Stanhope, 1997; Green & Kopelman, 2002) would hypothesise most forgetting occurs over relatively medium-term delays (i.e. within 30-minutes) after experimentally matching groups for initial learning with comparable forgetting rates thereafter.
    b. Others (e.g. Butler & Zeman, 2008b) would hypothesise the groups would exhibit comparable performance between short- and medium-term delays but that the TLE group would then exhibit

accelerated forgetting at relatively long-term delays (i.e. after at least one day).

Determination of which hypothesis is supported in the current study will be explored.

2. Participants with TLE will demonstrate accelerated forgetting on the route task after immediate learning.
    a. Some (e.g. Kopelman & Stanhope, 1997; Green & Kopelman, 2002) would hypothesise most forgetting occurs over relatively medium-term delays (i.e. within 30-minutes) after experimentally matching groups for initial learning with comparable forgetting rates thereafter.
    b. Others (e.g. Butler & Zeman, 2008b) would hypothesise the groups would exhibit comparable performance between short- and medium-term delays but that the TLE group would then exhibit accelerated forgetting at relatively long-term delays (i.e. after at least one day).

    Determination of which hypothesis is supported in the current study will be explored.

Further exploratory analysis will investigate possible relationships between different neuropsychological, questionnaire, and epilepsy-specific variables and forgetting rates on the above measures. Variables that have been highlighted in the literature as possibly influential in accelerated forgetting include: age, mood, age of onset of epilepsy, duration of epilepsy, laterality of seizure origin, presence of pathology on MRI scan, current seizure activity, seizure activity during the delay period, and anti-epileptic medication. Other relationships that would be interesting to explore include the relationship between long-term forgetting and: intelligence, performance on standardised memory measures, subjective memory ability, and subjective spatial navigation ability. These variables will be explored in an exploratory, rather than hypothesis-driven, fashion.

2. Measure Development

2.1 Task Characteristics

2.1.1 Nature of Material

A story (i.e. prose) task was developed as the verbal measure due to findings that story tasks are suitable to investigate long-term forgetting and have greater ecological validity than word list tasks (Butler & Zeman, 2008b; Baddeley et al., 2013). A measure suitable to assess accelerated long-term forgetting has recently been published with preliminary promising results (Baddeley et al., 2013). However, this Crimes Test has only been utilised in part (two out of four stories used) in one case study assessing accelerated long-term forgetting in TLE (Kemp et al., 2012). Piloting for the current study indicated that Baddeley's Crimes Test resulted in interference effects amongst control participants even after short delays, thus it was decided to develop a different story task, based on similar principles described by Baddeley et al. (2013), which were less likely to produce interference effects.

Additionally, a route video task was developed as the visuo-spatial measure due to its increased ecological validity in assessing spatial memory in real-life contexts compared to pen-and-paper visual memory measures (e.g. Barbeau et al., 2006; Tramoni et al., 2011). It has been suggested such measures may be more sensitive in the detection of difficulties in visuo-spatial memory which correlate more closely with patients' subjective memory complaints, thus could be of greater clinical utility when assessing visual memory (Plancher, Tirard, Gyselinck, Nicolas & Piolino, 2012).

2.1.2 Nature of Retrieval

The story task was deemed to be most appropriately assessed through cued recall (Baddeley et al., 2013). Considering the nature of making a spatial decision is typically a forced choice from a number of options, it was decided to assess recall on the visuo-spatial task with both forced-choice recognition of spatial decisions and cued recall of landmarks passed in the video following the spatial decision. This method was also thought to lend itself well to assessing recall by phone at later delays, due to responses being verbalised (rather than reliant on visuo-

construction) and the hypothesised ease of sending, and regulating access to, stills from the video. Telephone follow-up was a key element of the current design considering it was thought this would decrease attrition rates through increasing recruitment opportunities and reducing selection bias.

2.1.3 Time Frame

To establish a rate of forgetting at multiple testing intervals, a decision was made to assess recall at four intervals. It was decided to assess initial learning after 30-second (30s) delay with a distractor to minimise the influence of short-term memory boosting initial recall (Isaac & Mayes, 1999a, 1999b; Mulhert et al., 2011; Cowan, 1993). Recall after a medium-term delay was chosen to be after 10-minutes (10m) as this interval has been shown to be sensitive to measuring differences in initial retention of material (Green & Kopelman, 2002; Issac & Mayes, 1999a, 1999b; Kopelman & Stanhope, 1997). The first long-term recall delay was chosen to be at one-day (1d) as previous research has suggested accelerated forgetting may be most influential over the first 24-hour period (Mulhert et al., 2010; Martin et al., 1991; O'Connor et al., 1997). The second and final long-term delay was chosen to be after one week (1w) as previous research has suggested this delay is sufficient to detect accelerated long-term forgetting whilst minimising the potential for floor performance (Kemp et al., 2012; Manes et al., 2005).

2.2 Story Task Development

2.2.1 Pilot One

To avoid having to repeat recall at each delay point, giving opportunities for re-encoding, four separate stories were developed to assess at each delay. Extensive development and discussion with supervisors and collaborators was carried out to establish the materials and to ensure distinctiveness between trials to minimise retroactive and proactive interference. Initial piloting with eight control participants determined the optimal length for each story. Feedback and responses from participants additionally aided development of scoring criterion. An adapted story was subsequently piloted with nine control participants (Figure 1). One-sample t-tests were used to assess for ceiling effects at 30-second delay and floor effects at one-week delay. At 30-second delay, performance was significantly

different from 100%, indicating no ceiling effect, $t(8) = -7.633$, $p < .001$. At one-week delay, performance was significantly above 0%, indicating no floor effect, $t(8) = 5.328$, $p = .001$.

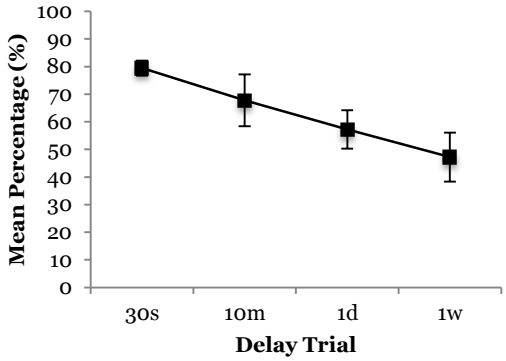


Figure 1: Pilot One: Control Participants' Long-Term Forgetting Performance

This pilot indicated that the story task developed avoided both ceiling and floor effects in control participants and avoided repeated recall of material at different delay points. Considering it met these methodological criteria it was also important to ascertain that each of the four story trials were equivalent to one another.

2.2.2 Pilot Two

This pilot aimed to establish equivalency across each of the four story trials. It was important to conduct this pilot as if the four trials were not equivalent in difficulty this would introduce variance in the data and confound interpretations of group differences. The story developed in the previous pilot (Appendix 1) was administered to 43 control participants in a counterbalanced order at the 30-second delay trial. The participant group consisted of 12 males and 31 females, with a mean age of 36 (S.D. = 13.98). They had an average of 17 years of education (S.D. = 2.89) and a mean NART-R FSIQ of 109.16 (S.D. = 7.40).

Participants who scored below two standard deviations of the group mean on any one story trial were excluded from data analysis (N = 4). Performance at 30-second delay across the four story trials is shown in Table 2. A one-way repeated measures ANOVA showed there was no significant difference between the four stories; $F(3,114) = 1.506$, $p = .217$. One-sample t-tests were used to assess for

ceiling effects on each of the story trials. These found that all trials were significantly different from ceiling (Table 2).

Table 2: Pilot Two: Control Participants' Performance on Each Story Trial

	Mean (S.D.)	t	p
Story A	79.36 (17.14)	-7.522	< .001*
Story B	80.77 (17.38)	-6.910	< .001*
Story C	79.49 (15.80)	-8.106	< .001*
Story D	74.87 (17.34)	-9.050	< .001*

*significant at .05

Conclusions from this pilot showed that each story trial was equivalent to one another and no individual story trial exhibited a ceiling effect. The presence of floor effects was not examined in this pilot as testing was limited to the 30-second delay trial.

2.3 Route Task Development

2.3.1 Pilot Three

To avoid having to repeat recall at each delay point, four individual route videos were developed to assess at each delay. Locations were selected based on the presence of sufficiently distinctive landmark cues within a relatively small distance to allow for reasonable presentation lengths. Each video was filmed using a GoPro fish-eye camera from the front of a moving car, driving through two English towns. Subsequent to the filming, modifications were made to the videos using FinalCutPro to pause at spatial decision points and at salient landmarks in the environment that followed these spatial decision points. For each trial, five spatial decision points and five landmark points were decided upon.

Stills of each spatial decision point were taken and formatted into a pdf file to use during the recall trials. Stills were shown in a sequential order during recall. The first still of a decision point had two numbers superimposed on the picture to indicate the possible directions the car drove from that point to give a two-option forced choice recognition format to the task. The following still was of the same decision point but without the superimposed numbers to enable a cued recall

question about a landmark passed following the decision point. An example of two of the stills used during recall for one decision point is shown in Figure 2.

(a) Spatial Decision Forced Choice Recognition
"Which way did we go from here: 1 or 2?"

(b) Landmark Cued Recall
"What is the name of the supermarket we passed after this turning?"

Figure 2: Example of Decision-Point Stills Used During Recall

To establish the feasibility of using this method to assess long-term visuo-spatial memory, this task was initially piloted with four control participants (Figure 3). One-sample t-tests were used to assess for ceiling effects at 30-second delay and floor effects at one-week delay. At 30-second delay, performance approached a significant difference from 100%, indicating the possibility of a ceiling effect, $t(3) = -3.181$, $p = .05$. At one-week delay, performance approached a significant difference from 25% (set at this level due to chance associated with the forced-choice recognition nature of the five spatial decision points), $t(3) = 3.087$, $p = .054$, indicating the possibility of a floor effect. However, it is worth noting that there was a high likelihood of finding a null result in this pilot due to the small sample size.

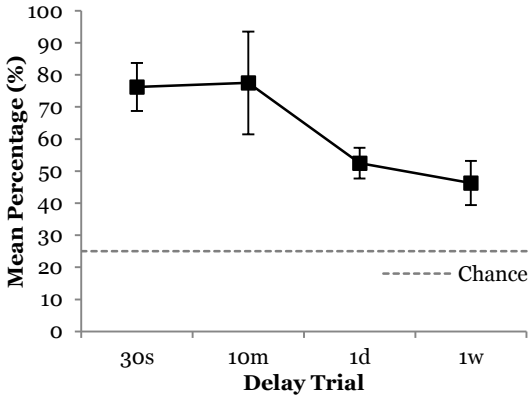


Figure 3: Pilot Three: Control Participants' Long-Term Forgetting Performance

Based on feedback from participants and observations made during piloting, modifications were made to decision points and the nature of the orienting questions was changed. Previously, participants' attention had been drawn to landmarks by asking participants a question relating to the landmark. However, after the pilot this strategy was changed and participants were told explicitly beforehand that they were required to remember landmarks passed during the journey and that their attention would be drawn to these. During the pause points participants' attention was drawn to the landmark with a statement such as "*Pay attention to this supermarket*". Following this, to ensure equivalency across all four route trials, a further pilot was carried out.

2.3.2 Pilot Four

This pilot aimed to establish equivalency across each of the four route trials. It was important to conduct this pilot as if the four trials were not equivalent in difficulty this would introduce variance in the data and confound interpretations of group differences. The route trials developed and modified in the previous pilot (Appendix 2) were administered to 27 control participants in a counterbalanced order at the 30-second delay trial. The participant group consisted of 8 males and 19 females, with a mean age of 28 (S.D. = 5.86). They had an average of 18 years of education (S.D. = 2.61) and a mean NART-R FSIQ of 109.67 (S.D. = 5.02).

Participants who scored below two standard deviations of the group mean on any one route trial were excluded from data analysis (N = 6). Performance at 30-second delay across the four route trials is shown in Table 3. A one-way repeated measures ANOVA of the total score showed there was no significant difference between the four routes; $F(3,60) = 2.223$, $p = 0.095$. One-sample t-tests were used to assess for ceiling effects on each of the route trials. All trials were found to be significantly different from ceiling (Table 3).

Table 3: Pilot Four: Control Participants' Performance on Each Route Trial

	Mean (S.D.)	t	p
Route A	89.29 (7.95)	-6.175	< .001*
Route B	87.38 (10.32)	-5.602	< .001*
Route C	91.67 (6.95)	-6.875	< .001*
Route D	92.38 (7.85)	-4.450	< .001*

*significant at .05

The outcome from this pilot indicated that the four route trials were equivalent to one another and no individual route trial exhibited a ceiling effect. The presence of floor effects was not examined in this pilot as testing was limited to the 30-second delay trial.

2.4 Matched Learning Between Groups

2.4.1 Participants with TLE Case Study

Many matching procedures have been discussed in the literature on long-term forgetting. Different procedures have included using prolonged exposure times (e.g. Huppert & Piercy, 1978, 1979; Kopelman, 1985; Kopelman & Stanhope, 1997; McKee & Squire, 1992) whilst others have used multiple presentations (e.g. Isaac & Mayes, 1999a). There is no evidence to suggest there is any difference between these two methods. Because the nature of the current study material (stories and routes) did not lend themselves to prolonged exposure, increasing the number of presentations was trialled in one patient recruited. This participant received two presentations of each trial before recall was assessed on both story and route measures. The other participant with TLE simply received one presentation to see how their performance compared to the controls recruited above.

The demographic and epilepsy-specific variables of the participants with TLE who took part in this pilot are shown in Table 4.

Table 4: Demographic and Clinical Variables of Pilot Participants with TLE

	Participant with TLE 1	Participant with TLE 2
Gender	Female	Female
Age (years)	54	60
Education (years)	15	13
NART-R FSIQ	119	114
Laterality	Right	Left
Last Seizure Before Appt.	4 months previously	Earlier that day
Seizures During Week	0	Approx. 14
Type of Seizures Experienced	Complex partial	Simple partial

The findings from this pilot were mixed (Table 5). Receiving one presentation on the story task was sufficient for this participant, whilst receiving two presentations may have resulted in overlearning for the other participant. Conversely, on the route task one presentation was not sufficient for matched performance with controls whilst two presentations were.

Table 5: Pilot Participants with TLE Long-Term Forgetting Performance

	Control Mean (S.D.)	Participant with TLE 1	Participant with TLE 2
Number of Trial Presentations	1	1	2
Story Task	**Percentage (%)**	**Percentage (%)**	**Percentage (%)**
30s	78.62 (16.91)	95	100
10m		80	80
1d		15	75
1w		0	20
Route Task			
30s	90.18 (8.45)	50	85
10m		80	80
1d		20	65
1w		20	20

This pilot highlighted the difficulty in deciding which matching procedure to use in accelerated long-term forgetting studies. However, it was clear that neither keeping the procedure identical to controls nor increasing the number of stimulus presentations was going to adequately match performance.

2.4.2 Matching Procedure

Butler and Zeman (2008b) have described a matching procedure whereby exposure to study material is ascertained on a case-by-case basis until a chosen learning criterion is reached. This criterion should be set at less than 100% as this

would be ceiling performance. This multiple presentation matching to criteria procedure has been used in previous research (Mulhert et al., 2011; Wilkinson et al., 2012; Evans et al., 2014) and was chosen to use currently based on the patient pilot results to ensure matched performance to controls whilst avoiding overlearning.

Thus, a learning criterion of 60% was set for the story task. This was based on Pilot Two's results that control participants performed at a mean of 79% with a standard deviation of 17%. One standard deviation below this mean was just over 60%. Ensuring learning to this criterion would guarantee participants did not perform significantly lower than control participants, whilst also avoiding overlearning.

Using a similar procedure, a learning criterion of 80% was set for the route task. This was based on Pilot Four's results that control participants performed at a mean of 90% with a standard deviation of 8%. Thus, one standard deviation below this mean was just over 80%. Ensuring learning to this criterion would guarantee participants did not perform significantly lower than control participants, whilst also avoiding overlearning.

Using this procedure, if a participant in either group did not perform at either 60% or 80% accuracy at the 30-second delay trial for either the story or route task respectively, this trial would be presented again and the 30-second recall trial repeated until this criterion was reached. Once the numbers of trials to reach criteria were established, this number of presentations of study material would be used in subsequent trials. Although this did mean that material was repeatedly recalled at the 30-second delay if the participant did not reach criteria on the first presentation, it avoided repeated recall at subsequent delays.

3. Case-Control Study Method

3.1 Ethical Review

Ethical approval for this study was given by the NHS National Research Ethics Service, London – Central and East Research Ethics Committee (REF: 13/LO/0399, Appendix 3). Research and Development (R&D) approval was subsequently approved across three sites: South London and Maudsley NHS Foundation Trust (SLaM); King's College Hospital NHS Foundation Trust (KCH); and Guy's and St Thomas' NHS Foundation Trust (GSTT). The Psychological Medicine Clinical Academic Group (CAG) and the Clinical Neurosciences CAG additionally gave approval for the study.

3.2 Design and Counterbalancing

Group differences on traditional neuropsychological tasks and questionnaires were analysed by comparing group means (TLE versus control [CON]). The recall performance of participants on the verbal (story) and visuo-spatial (route) tasks was examined by comparing independent group means (TLE versus CON) at each of the delay trials (30s, 10m, 1d, 1w). Recall performance was compared in a 2 (Group: TLE vs CON) x 4 (Trial: 30s, 10m, 1d, 1w) mixed model factorial design, with group as the between-subjects factor and trial as the within-subjects factor.

Order of trial presentation was counterbalanced across participants in both groups using diagram-balanced Latin squares (Keppel & Wickens, 2002). The presentation of each story or route trial was counterbalanced also, whereby half the participants were presented with story trials first and the other half presented with route trials first at each delay trial.

3.3 Participants

3.3.1 Sample Size Estimation

Power analysis was based on one previous study that examined accelerated forgetting using both verbal and visual forgetting measures in a sample of participants with TEA and healthy controls (Mulhert et al., 2010). This study measured recall of verbal (list learning) and visual (events that occurred in their life photographed using SenseCam, contiguous information preceding and

following this event, their thoughts about it and sensory recall) information at one-day, one-week and three-week delays. This study had a sample of 11 participants in each of the two groups. Using the data from the findings at one-day and one-week delay in this study, a power analysis was conducted using nQuery Advisor Version 4.0. Mulhert et al. found that, at one-day and one-week recall, there were significant differences between groups on list learning, contiguous event, and thought recall measures. The effect sizes (d) of these significant differences ranged between 1.00 and 2.00, which exceeded Cohen's (1992) threshold of 0.8 for a large effect size.

Although the majority of the effect sizes found in this study were greater than 1.20, a more conservative estimate of effect size was used for the current study considering the differences between measures used and patient groups. Estimating that the current study would also find a large effect size, between d = 1.00 and 1.20, a two sample t-test indicated that to detect a between-subjects difference of these sizes, with 80% power and an alpha level of 0.05, a sample size between 12 and 17 participants in each group for these effect sizes respectively would be required.

3.3.2 Groups

3.3.2.1 Clinical Group: Temporal Lobe Epilepsy

3.3.2.1.1 Recruitment

Eighteen participants were recruited from the Neuropsychiatry and Memory Disorders Service in SLaM, the Department of Clinical Neurosciences in KCH and the Department of Neurophysiology and Epilepsies in GSTT. At KCH and GSTT, patient records were screened for eligibility criteria by a clinician involved in their clinical care. Eligible patients were sent an introductory letter from their Consultant and asked to post back the reply slip provided if they were agreeable to be contacted by the Principal Investigator (Appendix 4). There was a 37% response rate across these sites. At SLaM, the Principal Investigator attended clinics held by two Consultant Neuropsychiatrists over a period of nine months and was introduced to eligible patients face-to-face. It was not possible to ascertain ineligibility information in SLaM because of the nature of these clinics and large

numbers of patients seen each week. Eligible patients across the three services who responded, or indicated that they were agreeable to further contact were then approached by the Principal Investigator and provided with verbal information about the study, given the opportunity to ask questions, and sent the Participant Information Sheet (Appendix 5). Patients who remained interested in participating were then contacted again to arrange an appointment to complete the research protocol. This appointment took place at either King's College Hospital (N = 9) or St Thomas' Hospital (N = 9). Figure 4 shows a flow diagram of the recruitment procedure across the three sites.

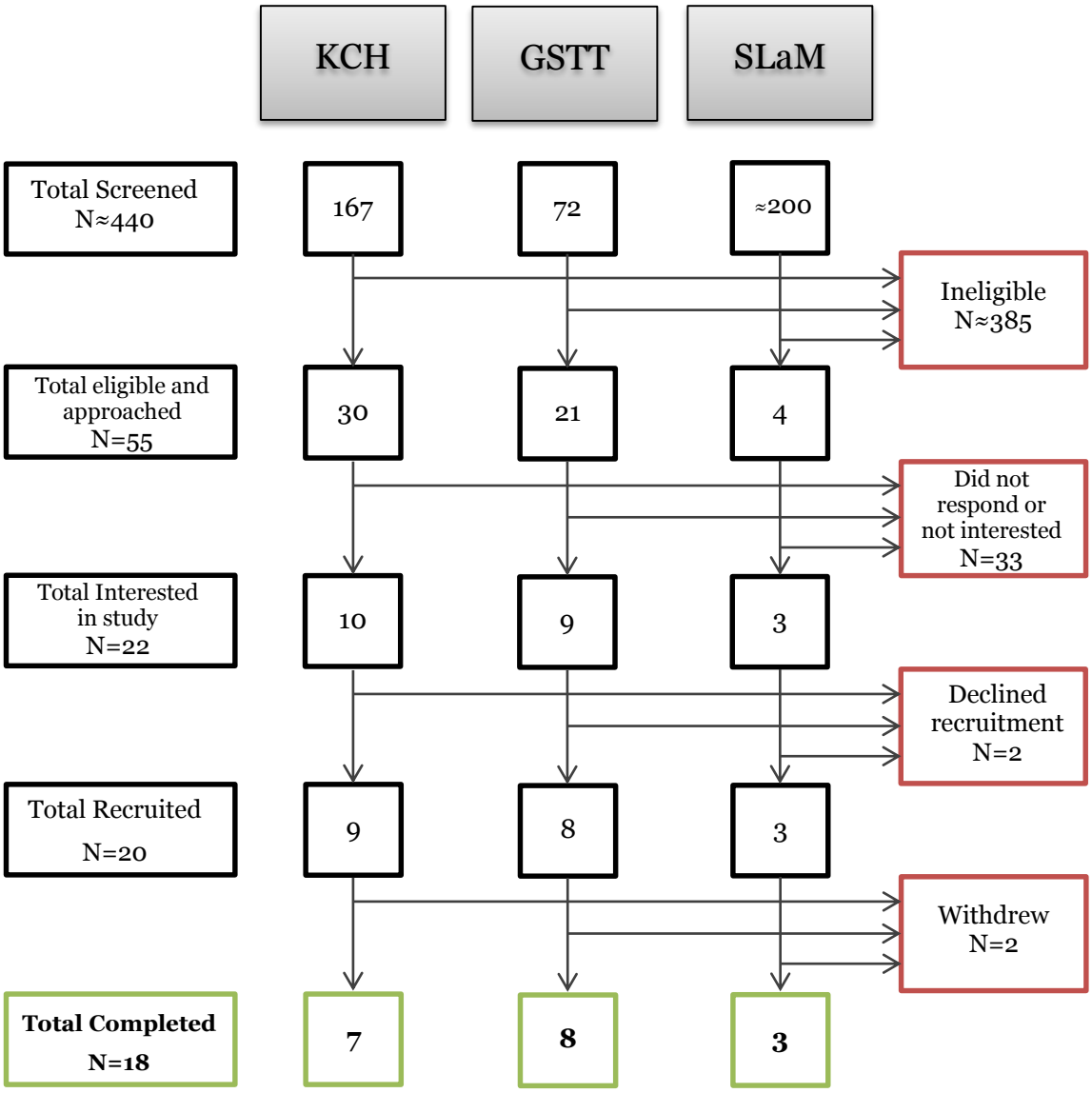


Figure 4: Flow Diagram of Participant Recruitment Across Sites

3.3.2.1.2 Eligibility Criteria

Patients meeting the following criteria were considered eligible for participation in the study:

- Aged 18 to 65 years
- Fluent with written and spoken English
- Clinical diagnosis of temporal lobe epilepsy made by a neurologist
- Had not undergone neurosurgery
- No history of cranial trauma or neurological disease, other than epilepsy
- No neurological damage or pathology outside of the temporal lobe
- No co-morbid major medical condition likely to affect cognitive performance
- No diagnosis of major psychiatric disorder
- No history of alcohol or substance misuse
- No history of learning disability or developmental disorder

Of the 188 patients screened at KCH and GSTT who were ineligible, reasons for ineligibility are shown in Table 6 (multiple reasons may apply).

Table 6: Reasons for Screened Patients' Ineligibility

	KCH	GSTT	SLaM
Outside age criteria	32	5	Unknown
Not fluent in English	7	8	
Other epilepsy diagnosis	43	8	
Undergone neurosurgery	5	6	
Other cranial trauma or neurological disease	5	4	
Pathology outside of temporal lobe	18	7	
Psychiatric comorbidity	9	7	
History of substance misuse	1	3	
Learning disability / Developmental disorder	14	3	
Other (e.g. deceased, lived abroad)	5	1	

3.3.2.2 Control Group: Healthy Controls

3.3.2.2.1 Recruitment

Eighteen participants were recruited from a participant database maintained by King's College London and the community. Potential participants who responded to the recruitment advertisement were screened for eligibility criteria either through e-mail or phone. Additionally, potential participants were screened for

their age, education and occupation (from which an estimate of their intelligence was made), and those who most closely matched the participants with TLE were selected to pursue. Those who met eligibility and matching criteria, and were interested in participating, were provided with verbal information about the study, given the opportunity to ask questions, and sent the Participant Information Sheet (Appendix 6). Those who remained interested in participating were then contacted again to arrange an appointment to complete the research protocol. This appointment took place at either St Thomas' Hospital in the Academic Neuropsychiatry Department (N = 8), the Institute of Psychiatry (N = 2), or the participant's workplace or home if they had access to a quiet room (N = 8).

3.3.2.2.2 Eligibility Criteria

Volunteers meeting the following criteria were considered eligible for participation in the study:

- Aged 18 to 65 years
- Fluent with written and spoken English
- No history of cranial trauma or neurological disease
- No major medical condition likely to affect cognitive performance
- No diagnosis of major psychiatric disorder
- No history of alcohol or substance misuse
- No history of learning disability or developmental disorder
- No subjective complaints of memory difficulties in everyday life

3.4 Measures

3.4.1 Forgetting Measures

3.4.1.1 Story Task

The story task developed for the current study is discussed in more detail in the previous chapter on measure development. The final task (Appendix 1), made up of four separate story trials, met the methodological aims of: (i) avoiding repeated testing of the same material; (ii) avoiding ceiling effects at 30-second delay; and (iii) avoiding floor effects at one-week delay amongst control participants. Each story had 13 units of information and was between 41 and 43 words in length. To

ensure standardised delivery, each story was recorded onto a laptop computer into an mp3 file. Each story took between 28 and 31 seconds to play.

Order of presentation of material at each delay was carried out in sequential order, i.e. 30-second recall was conducted first to establish number of presentations necessary for later trials. Presentation and recall for the 10-minute delay trial was then completed. One-day and one-week trial presentations were completed at the end of the research session. This protocol was developed not only to ensure accurate matching but also to minimise interference between story trials.

Participants were introduced to each story task with the instructions *"I am going to play you a story in a moment. I want you to listen carefully to the story and try to remember as much of it as you can. Do you have any questions?"*

The story was then played and depending on the delay trial the participant was then given different instructions. For 30-second recall, participants were asked to subtract serial threes from 100 as a distractor task for 30 seconds before the cued recall questions were asked. For 10-minute recall participants were told *"There's a little bit more time before I ask you questions about this story so we're going to do some other things in the meantime"*. Background neuropsychological assessment measures were completed during the 10-minute delay. For one-day and one-week recall, participants were told they would be asked questions about the respective story during the next week and asked not to rehearse the story during the week. The participant was telephoned one day and one week after trial presentation to complete the cued recall questions over the telephone.

3.4.1.2 Route Task

The route task developed for the current study is discussed in more detail in the previous chapter on measure development. The final task (Appendix 2), made up of four separate route video trials, met the methodological aims of: (i) avoiding repeated testing of the same material; and (ii) avoiding ceiling effects at 30-second delay. It was possible a floor effect may be observed based on Pilot Three's findings and so this was examined currently. Presentation was carried out through

an mp4 file on a laptop computer and took between one minute 38 seconds and two minutes one second to complete playing.

Order of presentation of material at each delay was carried out in sequential order, i.e. 30-second recall was conducted first to establish number of presentations necessary for later delays. Presentation and recall for the 10-minute delay trial was then completed. One-day and one-week trial presentations were completed at the end of the research session. This protocol was developed not only to ensure accurate matching but also to minimise interference between route trials.

Participants were introduced to each route task with the instructions *"I am going to play you a video of a car driving through a town in a moment. I want you to pretend you're a passenger in the car and pay attention to where we go and things we pass. Don't worry about remembering everything though, I'm going to pause the video at different points and draw your attention to the parts you need to remember. Do you have any questions?"* Each route trial was played and paused during administration at relevant points to draw the participant's attention to the direction the car travelled from that point and landmarks passed (Appendix 2).

Depending on the delay trial the participant was then given different instructions. For 30-second recall, participants were asked to attempt to separate two steel links from a puzzle for 30 seconds before the recall questions were asked. For 10-minute recall participants were told *"There's a little bit more time before I ask you questions about this route so we're going to do some other things in the meantime"*. Background neuropsychological assessment measures were completed during the 10-minute delay. For one-day and one-week recall, participants were told they would be asked questions about the respective route video during the next week and asked not to attempt to rehearse information learned during the week. Participants were asked for their email address and emailed the password-protected pdf file of decision point stills for the respective delay trials. Files were password protected to minimise the possibility of rehearsal. They were telephoned one day and one week after trial presentation, given the password to open the respective pdf file and completed the cued recall questions over the telephone.

3.4.2 Background Neuropsychological Measures

3.4.2.1 Predicted Intellectual Functioning

The National Adult Reading Test - Revised Version (NART; Nelson & Willison, 1991) was used to estimate the participants' level of intellectual functioning. Estimated intellectual functioning is determined from the number of errors participants' made on the task, and has been shown to be resistant to wider cognitive changes in people with mild neurological impairment (Bright, Jaldow & Kopelman, 2002; Crawford, Parker & Besson, 1988; Watt & O'Carroll, 1999; Moss & Dowd, 1991), thus would provide a premorbid estimate of intelligence in those participants with adult-onset epilepsy. The NART has been shown to have good reliability and convergent validity (e.g. O'Carroll, 1995; Crawford, Deary, Starr & Whalley, 2001).

3.4.2.2 Intellectual Functioning

The Vocabulary and Matrix Reasoning subtests from the Wechsler Abbreviated Scale of Intelligence – Second Edition (WASI-II; Wechsler, 2011) were used to calculate participants' Full Scale Intelligence Quotient – Two Subtests (FSIQ-2). The reliability coefficient of the FSIQ-2 has been shown to be excellent (r = .94) and this measure has established concurrent validity with other measures of intelligence (Wechsler, 2011; McCrimmon & Smith, 2013).

3.4.2.3 Memory

The Word Lists I and II and Visual Reproduction I and II subtests from the Wechsler Memory Scale – Third Edition, UK Adaptation (WMS-III^{UK}; Wechsler, 1997) were used to measure anterograde verbal and visual immediate and delayed memory. These particular subtests were chosen so that any interference with the experimental forgetting tasks was minimised. Individual subtests have also been shown to have high internal consistency (between .74 and .93), inter-rater reliability, and established discriminant validity (Groth-Marnat, 2003).

3.4.2.4 Executive Functioning

The Hayling and Brixton tests (Burgess & Shallice, 1997) were chosen as measures of executive functioning. The Hayling test provides a measure of task initiation speed and response inhibition in two sections. The Brixton test provides a measure

of one's ability to detect and follow rules, and rule-switching flexibility. The Hayling and Brixton tests have been shown to have good reliability (Burgess & Shallice, 1997) and convergent validity (e.g. Marczewski, van der Linden & Laroi, 2001).

3.4.2.5 Naming

The Graded Naming Test (GNT; McKenna & Warrington, 1983) was chosen as a measure of pictorial naming ability. This measure has been shown to have good reliability (Bird & Cipolotti, 2007) and convergent validity with word reading measures and vocabulary ability (McKenna & Warrington, 1983).

3.4.3 Questionnaires

3.4.3.1 Subjective Memory in Everyday Life

The Everyday Memory Questionnaire – Revised Version (EMQ-R; Royle & Lincoln, 2008; Sunderland et al., 1983) was used as a 13-item self-report measure of participants' experiences of memory failure in everyday life. This measure has been shown to have good internal reliability and discriminatory properties (Royle & Lincoln, 2008).

3.4.3.2 Subjective Spatial Navigation

The Santa Barbara Sense of Direction Scale (SBSOD; Hegarty, Richardson, Montello, Lovelace & Subbiah, 2002) was used as a 15-item self-report measure of participants' environmental spatial abilities. This measure has been shown to have good reliability and internal consistency (Hegarty et al., 2002).

3.4.3.3 Mood

The Beck Depression Inventory – Second Edition (BDI-II; Beck, Steer & Brown, 1996) was used as a 21-item self-report measure of participants' mood over the preceding two weeks. This measure has been shown to have high internal consistency and construct validity (Beck et al., 1996).

3.4.3.4 Anxiety

The Beck Anxiety Inventory (BAI; Beck & Steer, 1993) was used as a 21-item self-report measure of participants' experience of anxiety over the preceding week.

This measure has been shown to have high internal consistency (Beck, Epstein, Brown & Steer, 1988) and validity (e.g. Fydrich, Dowdall & Chambless, 1990).

3.5 Procedure

3.5.1 Overview

All participants gave informed consent at the beginning of the research session (Appendix 7). They were informed that the aim of the study was to investigate long-term forgetting in people with TLE and were invited to ask questions before beginning the assessment. The research session typically lasted between 1.5 and two hours and participants completed the neuropsychological assessment, two trials of the story and route forgetting measures (at 30-second and 10-minute delays) and were presented with the information of the remaining two trials. This session took place at St Thomas' Hospital, King's College Hospital, the Institute of Psychiatry, or the participant's workplace or home, depending on participant request. At the end of the research session participants were thanked for their time and support, and reimbursed for their travel costs at a flat rate of £10 per session. Participants were emailed the files for one-day and one-week route trials and telephoned one day and one week after this to complete the remaining two trials of the forgetting measures. At the end of the second phone call, participants were thanked again for their participation and participants with TLE were asked about seizure activity during the past week. It is worth noting that having access to the internet was not an explicit inclusion criterion for the study but all participants were able to access the emailed files.

3.5.2 Research Session

3.5.2.1 Interview

Following informed consent, the research session began with participants providing information about their demographic characteristics. Participants with TLE were asked questions concerning their epilepsy, including their last seizure before the appointment, the type, frequency and duration of seizures, and current antiepileptic medication. This information, in addition to documentation of neurophysiology and scan investigations, was later corroborated from participants' medical records.

3.5.2.2 Forgetting Measures

Participants completed the 30-second delay trials of the story and route forgetting tasks as the first measure completed during the session. Performance on the 30-second delay trial dictated the number of presentations the participant would receive; if the participant scored below 60% on the story trial or 80% on the route trial, presentation was repeated. There was no limit on the number of presentations required to reach criterion for the story trial but due to the length of time route presentation took, it was decided to only repeat presentation a maximum of two times for this task. The number of presentations required until learning criterion was reached was then used in later trials for the respective measure.

Following 30-second recall and determination of the number of presentations required during the remaining trials, the story and route trials for 10-minute recall were presented to the participant. During the 10-minute delay, participants completed tasks from the background neuropsychological assessment battery and some of the questionnaire measures, within time allowances.

Following 10-minute recall, the background neuropsychological assessment was administered. On completion of this background battery, the remaining trials were presented to the participant. One-day recall trials were presented first, followed by the one-week recall trials. Participants were informed they would be contacted by phone to complete these delay trials, they were asked for their email address, and a convenient time was made to call them one day and one week following the research session.

3.5.2.3 Neuropsychological Assessment

The order in which the participant completed each of the neuropsychological assessment tasks was identical for all participants; the NART, GNT, and EMQ-R and SBSOD questionnaires (questionnaire completion was dependent on time available) were completed during the 10-minute recall delay of the forgetting measures. After the 10-minute recall trials were completed, participants were offered a break. Following this, the Word Lists I and Visual Reproduction I subtests from the WMS-III were completed. The Vocabulary and Matrix Reasoning subtests

from the WASI-II were administered during the 25 to 35 minute delay period before the delayed memory tasks from the WMS-III (Word Lists II and Visual Reproduction II) were completed. Finally, participants completed any outstanding questionnaires, including the BDI-II and BAI, and then the Hayling and Brixton tests. The remaining two trials of the forgetting measures were then presented to the participant before finishing.

3.5.3 Follow-Up Phone Calls

A convenient time was arranged with participants, during the research session, to call them one day and one week following the appointment. Before their first phone call, participants were emailed the files to open corresponding to their respective route trial at one-day and one-week recall but were not given the password to open the file until the phone call. Participants were telephoned at the time arranged one day and one week following the research session and completed the one-day and one-week recall questions for each of the forgetting measures. Following completion of the recall questions after one week, participants with TLE were asked about any seizures experienced during the week since the research session. All participants were thanked again for their participation.

4. Results

4.1 Overview of Results

In this chapter, initially the background demographic, neuropsychological and questionnaire data will be presented. Secondly, the results from the analyses of the forgetting measures will be described in the order of the hypotheses presented in the Introduction. Finally, the relationships between clinical variables, background neuropsychological test scores (where appropriate), and forgetting rates will be explored.

4.2 Planned Statistical Analyses and Sampling Distributions

Data were analysed using IBM SPSS 22.0 for Mac OS X. Descriptive statistics were produced and raw data were checked using box plots and histograms for normal distribution and outliers. Although it was anticipated there would be a skew in some of the data points (e.g. at 30-second recall delay for the forgetting measures), if the variance at the delay trial between groups did not differ noticeably, parametric analyses were used in view of their greater power to reject the null hypothesis (Howell, 2012). Decisions regarding normality were made based on these checks and advice from a statistician at the Institute of Psychiatry, King's College London. Where data deviated from normal distribution, non-parametric alternatives to parametric analyses were used. The primary hypotheses were conducted using a mixed-model two-way analysis of variance (ANOVA) comparing forgetting rates between groups. The relationships between clinical variables, neuropsychological test performance and forgetting rates were examined using correlational analyses for continuous variables and independent samples comparisons for categorical data.

4.3 Level of Significance and Standardised Data

For the comparison between demographic and neuropsychological variables, and the primary dependent variable of forgetting rate over a week period an alpha level was set at .05. However, considering the number of post-hoc and exploratory analyses that were planned, the criterion for significance was adjusted for these exploratory analyses to an alpha level of .01. This alpha level was chosen based on previous research that used this alpha level for secondary analyses (e.g. Evans et

al., 2014) considering Bonferroni corrections were likely to be too conservative for the purposes of the current study.

In relation to the background standardised neuropsychological data, where possible group differences were calculated and displayed using z scores and effect sizes. Z scores indicate the number of standard deviations above or below the control group mean that the patient group perform and effect sizes were calculated using Cohen's d (Cohen, 1992). Effect sizes were interpreted using Cohen's guidelines that indicate small (0.2), medium (0.5) and large (0.8) differences between groups.

4.4 Demographic Information

There were 18 participants in both the TLE and CON groups. The groups were matched for age, gender, years of full-time education, and estimated FSIQ (Table 7).

Table 7: Demographic Characteristics of TLE and CON sample

	Mean (SD)		Statistic	p
	TLE	**CON**		
Gender (M:F)	9:9	9:9	$\chi^2 = .000$	1.000
Age (years)	39.33 (9.80)	39.67 (13.27)	$t(34) = -.086$	.932
Education (years)	15.06 (2.84)	15.00 (2.97)	$t(34) = .057$	.955
Estimated FSIQ (NART-R)	108.50 (10.08)	106.39 (9.36)	$t(34) = .651$	.519

4.5 Clinical Variables

Table 8 displays the clinical variables for each of the 18 TLE participants.

4.5.1 Age of Onset

Participants in the TLE group developed epilepsy at a mean age of 20.33 (S.D. = 10.24), with a range of onset between the ages of 1 and 39. Seven participants developed TLE under the age of 18, whilst 11 developed adult-onset TLE.

4.5.2 Duration of TLE

Participants in the TLE group had lived with epilepsy for an average of 19 years (S.D. = 9.80) prior to the assessment, with a range between 3 and 38 years.

4.5.3 Seizure Type

Participants experienced a range of seizures across the spectrum from simple partial seizures to secondary generalised tonic clonic seizures. Five participants had only experienced complex partial seizures and 13 had experienced at least one secondary generalised seizure in the past.

4.5.4 Current Seizure Activity

Four participants had not experienced any seizures during the past six months. Unfortunately, it was not possible to reliably establish the frequency and type of seizures participants commonly experienced as this information was not readily available from clinical notes and some participants could not always give a reliable account of their recent seizure activity.

Five participants experienced seizures during the week of participation. Two participants experienced seizures by both one-day and one-week delay (one experienced a number of simple partial seizures, one experienced complex partial seizures). Three participants experienced one seizure between one-day and one-week delay (one simple partial, one complex partial, and one secondary generalised).

4.5.5 Medication

One participant was not prescribed any AED. Of the remaining 17 participants, nine were prescribed one AED, six were prescribed two AEDs, and two were prescribed three AEDs.

4.5.6 Lateralisation on EEG

EEG data were available for 16 participants. Conclusions from EEG recordings implicated left-hemisphere seizure origin for six participants, right-hemisphere seizure origin for six participants, and bilateral-hemisphere seizure origin for four participants.

4.5.7 Pathology on MRI

MRI data were available for 16 participants. 'Normal' MRI findings were reported for 12 participants, mesial temporal sclerosis was noted for three participants: one bilaterally, one in the left hemisphere, and one in the right hemisphere. One participant had evidence of left-hemisphere hippocampal abnormality, which was presumably of congenital origin.

Table 8: Clinical Variables of Participants with TLE

ID	Age	Gender	Age of Onset	Duration (years)	Seizure Types	Seizure Activity in Past Six Months	Medication	Laterality (EEG)	MRI	Seizure Activity During Week	No. Story Learning Trials	No. Route Learning Trials
1	40	M	36	4	SPS; GTC	N	CBZ	Bilateral	Unknown	N	1	1
2	35	F	15	20	CPS	Y	CBZ; LCM	R	Normal	N	1	1
3	50	F	31	19	CPS; GTC	N	LCM	Bilateral	L MTS	N	1	2
4	48	M	39	9	CPS	Y	LTG	Unknown	Unknown	N	1	1
5	21	M	1	20	CPS; GTC	Y	CBZ; LTG; BMZ	R	Normal	Y: CPS, GTC	2	1
6	51	F	13	38	SPS; CPS; GTC	N	SVP	L	Normal	N	1	1
7	19	F	11	8	CPS	Y	LEV; CBZ	L	Normal	N	1	1
8	36	M	16	20	CPS; GTC	Y	LTG; LEV	L	CG L HC Abnormal	Y: CPS	2	1
9	53	M	24	29	CPS	Y	LEV; CBZ	Bilateral	Bilateral MTS	N	2	1
10	48	F	27	21	SPS; CPS; GTC	Y	None	R	Normal	Y: SPS	1	1
11	38	F	22	16	SPS; GTC	N	LEV	Unknown	Normal	N	1	1
12	39	M	32	7	CPS; GTC	Y	CBZ	L	Normal	N	1	1
13	38	F	4	34	SPS; CPS; GTC	Y	LEV; LCM	R	R MTS	Y: CPS	2	2
14	25	M	22	3	SPS; GTC	Y	CBZ-CR	L	Normal	N	1	1
15	45	F	21	24	SPS; GTC	Y	CLB; LTG; LCM	R	Normal	N	2	2
16	40	F	18	22	SPS; GTC	Y	LTG	L	Normal	Y: SPS	2	1
17	38	M	14	24	SPS; CPS; GTC	Y	OXC	R	Normal	N	1	1
18	44	M	20	24	CPS	Y	LTG; CBZ	Bilateral	Normal	N	1	1

Index: BMZ = Buccal midazolam, CBZ = Carbamazepine, CBZ-CR = Carbamazepine retard, CG = Congenital, CLB = Clobazam, CPS = complex partial seizures, EEG = electroencephalography; F = female, GTC = generalised tonic clonic, HC = Hippocampus, L = Left, LCM = Lacosamide, LEV = Levetiracetam, LTG = Lamotrigine, M = male, MRI = magnetic resonance imaging, MTS = mesial temporal sclerosis, N = no, OXC = Oxcarbazepine, R = Right, SPS = simple partial seizures, SVP = Sodium valproate, Y = yes

4.6 Neuropsychological Profiles

All participants completed a battery of background neuropsychological assessments (Table 9). The cognitive profile of the group with TLE is presented as effect sizes and z scores compared to the control group. On most measures a higher score is indicative of better performance, with the exception of the Brixton task where a lower score is indicative of fewer errors, thus better performance.

Participants with TLE did not differ significantly from controls on a brief measure of FSIQ. Similarly, there were no significant differences between groups on measures of verbal and visual immediate memory (Word Lists I and Visual Reproduction I) or on measures of verbal and visual delayed recall (Word Lists II and Visual Reproduction II). Additionally, there were no significant differences between groups on measures of executive functioning or on a measure of object naming.

Table 9: Background Neuropsychological Test Performance

Neuropsychological Variable	Mean (S.D.) / Median (IQR)		Statistic	p	z score	Effect size (d)
	TLE	CON				
INTELLECTUAL FUNCTIONING						
WASI-II FSIQ-2	107.78 (13.21)	106 (9.91)	t(34) = .457	.651	+0.18	0.15
MEMORY						
WMS-III						
WL I	32.39 (7.04)	34.89 (4.65)	t(34) = -1.257	.217	-0.54	0.42
WL II Recall	6.78 (3.54)	8.39 (2.28)	t(34) = -1.623	.114	-0.71	0.54
VR I	83.22 (14.13)	86.39 (15.43)	t(34) = -.642	.525	-0.21	0.21
VR II Recall	59.83 (29.00)	67.22 (20.36)	t(34) = -.885	.382	-0.36	0.29
EXECUTIVE FUNCTIONING						
Hayling Composite	18.5 (16.25 – 19.75)	19 (18.25 – 20)	U = 211.50	.118	-1.23	0.69
Brixton	14.89 (7.88)	12.28 (5.93)	t(34) = .381	.269	+0.44	0.37
NAMING						
GNT	20.22 (5.14)	19.22 (3.49)	t(34) =.246	.499	+0.29	0.23

Although there were no significant differences between the groups on standardised memory measures, a sub-set of participants with TLE exhibited 'impaired' or 'borderline' performance on verbal (N = 1 [impaired]) and visual (N = 1 [impaired], N = 3 [borderline]) delayed memory measures, which was not observed in the control group. This suggests that a minority of participants with TLE did exhibit deficits on standardised memory measures.

4.7 Self-Report Questionnaires

All participants completed self-report questionnaires measuring depression, anxiety, subjective everyday memory performance and spatial navigation abilities. The raw scores on these measures are presented alongside effect sizes and z scores compared to the control group (Table 10). On mood measures (BDI-II and BAI) a higher score indicates greater symptom severity; on the everyday memory questionnaire (EMQ-R) a higher score indicates greater perceived difficulties; and on the spatial navigation questionnaire (SBSOD) a higher score is indicative of better subjective spatial navigation abilities.

Participants with TLE reported significantly more symptoms of depression than controls, with a large effect size (d = 0.96). Even so, this median score is still within the 'minimal' range of clinical depression. Three participants with TLE scored within the 'mild' range, three within the 'moderate' range, and three within the 'severe' range of depression whilst two participants in the control group scored within the 'moderate' range. There was no significant difference in symptoms of anxiety reported between groups. Participants with TLE reported significantly more everyday memory difficulties than controls and also reported significantly worse spatial navigational abilities than controls, with large effect sizes (d = 1.25 and 1.13 respectively).

Table 10: Questionnaire Ratings

Questionnaire Variable	Mean (S.D.) / Median (IQR)		Statistic	p	z score	Effect size (d)
	TLE	CON				
Depression (BDI-II)	13.50 (3 – 23.75)	2.50 (1 – 5)	U = 81.50	.010*	+2.22	0.96
Anxiety (BAI)	5.50 (0.25 – 13.25)	3 (2 – 8)	U = 156.50	.864	+0.52	0.35
Everyday Memory (EMQ-R)	26.89 (16.47)	11.22 (6.45)	t(34) = 3.76	.001*	+2.43	1.25
Spatial Navigation (SBSOD)	51.67 (19.32)	70.83 (14.27)	t(34) = -3.39	.002*	-1.34	1.13

*significant at .05

4.8 Ceiling and Floor Effects

To determine that the tasks avoided both ceiling and floor effects, one-sample t-tests were conducted at the first recall delay (30-seconds) and last recall delay (one-week). Ceiling (i.e. performance was significantly different from 100%) and floor (i.e. performance was significantly different from 0% on the story task and 25% on the route task) effects were avoided in both story and route tasks in both TLE and control groups (Table 11).

Table 11: Ceiling and Floor Effects of Forgetting Measures

		t(17)	p
Story Task			
30s	**TLE**	-6.351	<.001*
	CON	-7.261	<.001*
1w	**TLE**	6.016	<.001*
	CON	7.498	<.001*
Route Task			
30s	**TLE**	-6.168	< .001*
	CON	-4.461	< .001*
1w	**TLE**	3.198	.005*
	CON	5.712	< .001*

*significant at .05

4.9 Story Task

The first hypothesis of the current study related to whether participants with TLE displayed accelerated forgetting on the story task after matching performance with control participants at 30-second delay and, if so, at which delay this occurred.

Six TLE participants required two presentations to reach learning criterion of 60% on the story task. No control participants required two presentations.

A mixed-model two-way ANOVA with group as the between-subjects factor (TLE vs CON) and delay trial as the within-subjects factor (30s, 10m, 1d, and 1w) was used to investigate long-term forgetting. The ANOVA indicated a significant main effect of group, $F(1,34) = 6.782$, $p = .014$, and a significant main effect of delay, $F(3,102) = 99.671$, $p < .001$. There was additionally a significant delay-by-group interaction, $F(3,102) = 2.929$, $p = .037$. This indicates that there was accelerated

long-term forgetting in the TLE group compared with controls; Figure 5(a) shows performance at different delays on this task.

Pairwise between-group t-test comparisons at each delay were subsequently conducted to establish at which delay accelerated forgetting occurred. Using the adjusted alpha level of .01, the only significant difference between groups was found at one-week delay, $t(34) = -3.741$, $p = .001$. Figure 5(a) displays each group's z scores and effect size of the difference between groups at each delay.

4.10 Route Task

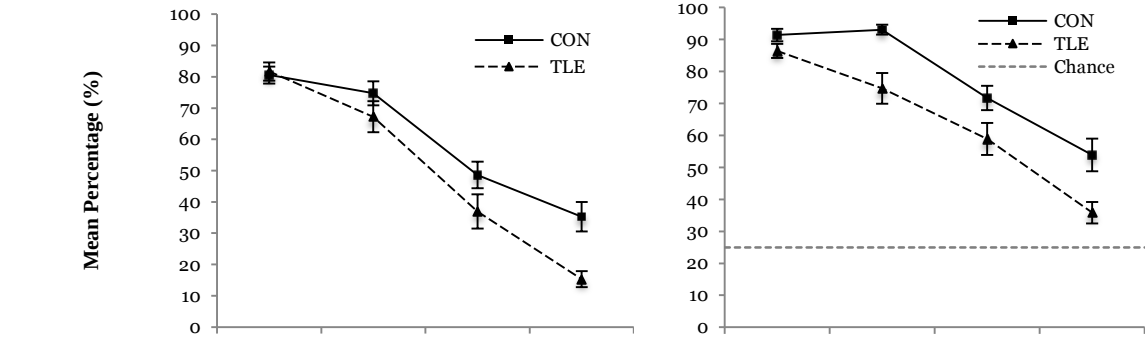
The second hypothesis of the current study related to whether participants with TLE displayed accelerated forgetting on the route task after matching performance with control participants at 30-second delay, and if so, at which delay this occurred.

Three TLE participants required two presentations to reach learning criterion on the route task. One control participant also required two presentations of material.

A mixed-model two-way ANOVA with group as the between-subjects factor (TLE vs CON) and delay trial as the within-subjects factor (30s, 10m, 1d, and 1w) was used to investigate long-term forgetting. The ANOVA indicated a significant main effect of group, $F(1,34) = 18.374$, $p < .001$, and a significant main effect of delay, $F(3,102) = 68.061$, $p < .001$. There was however no significant delay-by-group interaction, $F(3,102) = 1.655$, $p = .182$.

However, visual inspection of Figure 5(b) suggested that participants with TLE displayed most forgetting over the medium-term, 10-minute, delay whilst control participants did not exhibit decay in performance (this pattern of control performance was also noted in Pilot Three). Analysis of paired contrasts revealed a significant interaction between 30-second and 10-minute delay, $F(1,34) = 7.253$, $p = .011$, no significant interaction between 10-minute to one-day delay, $F(1,34) = .697$, $p = .410$, and no significant interaction between one-day and one-week delay, $F(1,34) = .448$, $p = .508$. Figure 5(b) also shows the z scores and effect sizes of the difference between groups at each delay, which corroborate this finding. This

suggested that there was accelerated medium-term forgetting in the TLE group compared to controls over a 10-minute delay but that forgetting was not accelerated compared to controls over the long-term delays.



		(a) Story Task				(b) Route Task			
		30s	**10m**	**1d**	**1w**	**30s**	**10m**	**1d**	**1w**
CON	**Mean**	80.56	74.72	48.61	35.28	91.29	93.06	71.67	53.89
(N=18)	**S.D.**	11.36	16.40	18.13	19.96	8.19	6.67	16.18	21.46
TLE	**Mean**	81.67	67.22	36.94	15.28	86.39	74.72	58.89	35.83
(N=18)	**S.D.**	12.25	21.16	23.34	10.77	9.36	20.33	21.18	14.37
	t(34)	.282	-1.189	-1.675	-3.741	-1.705	-3.636	-2.034	-2.966
	p	.780	.243	.103	.001*	.097	.001*	.050	.005*
	z score	+0.10	-0.46	-0.64	-1.00	-0.60	-2.75	-0.79	-0.84
	d	0.09	0.40	0.56	1.25	0.56	1.21	0.68	0.99

*significant at .01

Figure 5: Between-Group Long-Term Forgetting Performance on Story and Route Tasks with Descriptive Statistics, Z Scores and Effect Sizes of the Between-Group Difference at Each Delay

4.11 Exploratory Analyses

4.11.1 Variables That May Influence Forgetting Rate

The variables that have been highlighted in the literature that may influence forgetting rates include: age, age of onset of epilepsy, duration of epilepsy, mood, laterality of seizure origin, presence of pathology on MRI scan, current seizure activity, seizure activity during the delay period, and anti-epileptic medication.

Where appropriate, participants with TLE were categorised into sub-groups to explore these variables further. Sub-group exploration was carried out categorising participants with: (i) confirmed left-hemisphere versus right-hemisphere seizure laterality; (ii) presence of seizure activity within the past six months versus no seizure activity; (iii) presence of seizure activity during the delay period versus no seizure activity; (iv) presence of pathology on MRI scan versus 'normal' scan; and (v) monotherapy versus polytherapy AED treatment.

Graphs were plotted exploring forgetting rates over the week-period for each of these sub-groups (Figure 6). Effect sizes were calculated and where a large effect size was found (d ≥ .80) statistical analyses were carried out to investigate the strength of the statistical interaction. However, further statistical analyses were avoided considering the small sample sizes in each sub-group, which reduced the power of statistical analyses to detect a significant result.

Participant age, age of onset of epilepsy, duration of epilepsy, and mood (i.e. score on BDI-II and BAI), which were continuous variables, were explored using Pearson's bivariate correlational analyses at each delay trial. Where there appeared to be a significant correlation between these variables and recall score, the variable was entered into an analysis of covariance to examine its influence on forgetting rate.

4.11.1.1 Laterality of Seizure Focus

On the story task, laterality of seizure focus was not associated with forgetting rate.

Interestingly, on the route task, laterality was not associated with forgetting at the first three delays but at one-week delay, participants with right-hemisphere laterality of seizure origin performed worse than those with left-hemisphere laterality (d = 1.80). Analysis of this contrast revealed no significant interaction between one-day and one-week delay, $F(1,10) = 1.509$, p = .247. However, an independent-samples t-test of the difference between left- and right-hemisphere lateralisation at one-week delay approached significance, $t(10) = 3.124$, p = .011.

4.11.1.2 Current Seizure Activity

On the story task, experience of seizures during the past six months was associated with poorer recall only at 10-minute delay (d = 0.80). Analysis of this contrast revealed no significant interaction between 30-second and 10-minute delay, $F(1,16) = .359$, p = .539.

Conversely, on the route task, experience of seizures during the past six months was associated with poorer recall only at one-day delay (d = 0.86). Analysis of this contrast revealed no significant interaction between 10-minute and one-day delay, $F(1,16) = .529$, p = .478.

Experience of seizures during the experimental delay week was not associated with forgetting on either the story or the route task.

4.11.1.3 Pathology on MRI Scan

On the story task, presence of MTL pathology on MRI scan was associated with poorer recall at 10-minutes and one-week (d = 1.34 and 1.20 respectively). Interestingly, at one-day recall, MTL pathology was not associated with poorer recall (d = 0.23). Analysis of these contrasts approached significance between 30-second and 10-minute delay, $F(1,14) = 7.604$, p = .015, but was not significant between one-day and one-week delay, $F(1,14) = .325$, p = .577. Independent-sample t-tests at 10-minute and one-week delays approached significance, $t(14) = -2.329$, p = .035, and $t(14) = -2.084$, p = .056 respectively.

On the route task, presence of MTL pathology on MRI scan was associated with poorer recall at 10-minutes only (d = 1.01). Analysis of this contrast revealed no significant interaction between 30-second and 10-minute delay, $F(1,14) = 1.718$, p = .211.

4.11.1.4 Anti-Epileptic Medication

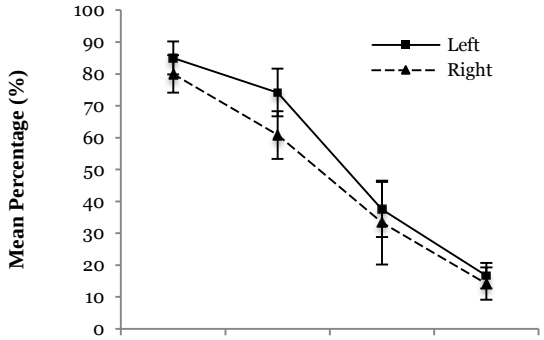
On the story task, polytherapy drug treatment for epilepsy (as opposed to monotherapy) was associated with poorer recall only at 10-minutes (d = 1.56). Analysis of this contrast approached significance between 30-second and 10-minute delay, $F(1,15) = 4.483$, p = .051. Further, an independent-samples t-test of the difference between participants on monotherapy versus polytherapy at 10-minute delay was significant, $t(15) = 3.211$, p = .006.

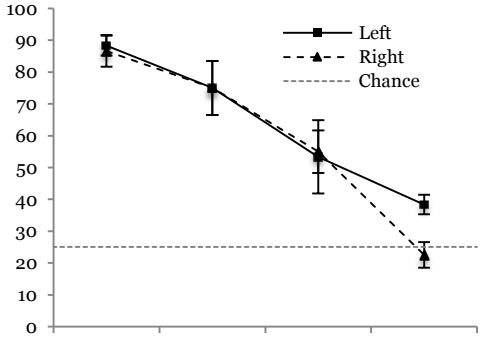
On the route task, polytherapy drug treatment for epilepsy (as opposed to monotherapy) was associated with poorer recall at both 30-second and 10-minute delays (d = 0.91 and 0.92 respectively). Analysis of this contrast revealed no

significant interaction between 30-second and 10-minute delay, $F(1,15) = 1.052$, $p = .321$.

Story Task | **Route Task**

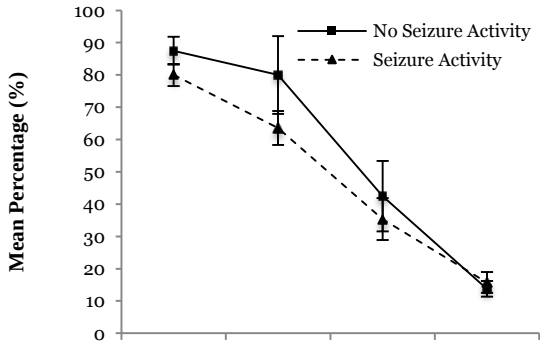
Laterality of Seizure Focus

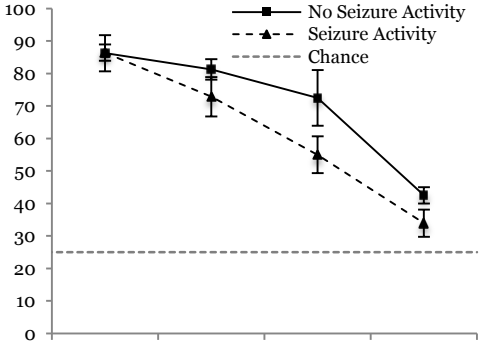




		30s	10m	1d	1w	30s	10m	1d	1w
Left	**Mean**	85.00	74.17	37.50	16.67	88.33	75.00	53.33	38.33
(N=6)	**S.D.**	12.65	18.28	21.15	9.83	7.53	20.74	28.23	7.53
Right	**Mean**	80	60.83	33.33	14.17	86.67	75.00	55.00	22.50
(N=6)	**S.D.**	14.49	18.28	32.20	12.42	12.12	20.74	16.43	9.87
	d	0.37	0.73	0.15	0.22	0.16	0	0.07	1.80*

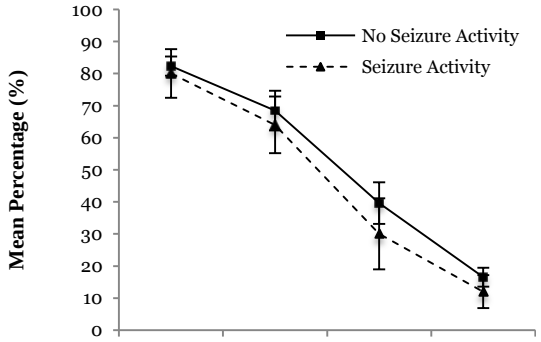
Seizure Activity within Past Six Months

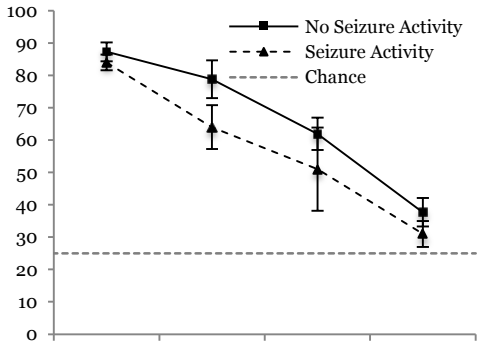




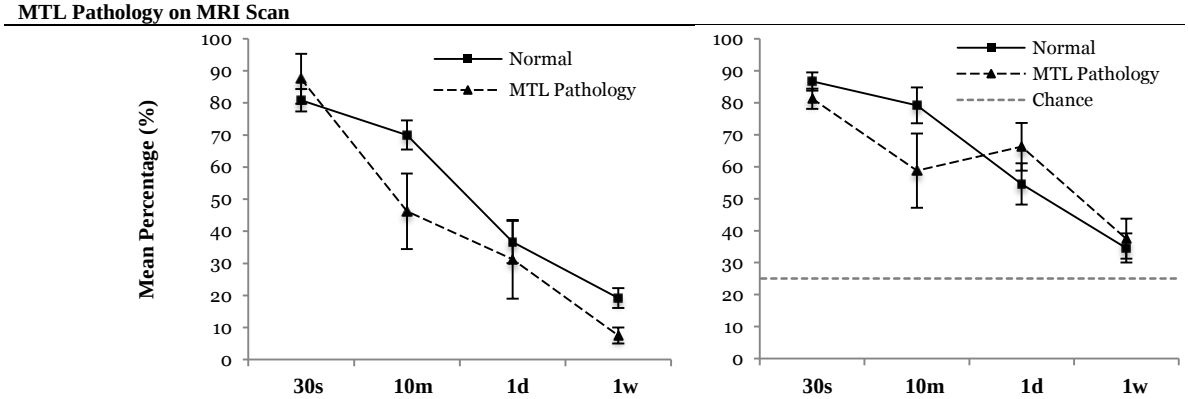
		30s	10m	1d	1w	30s	10m	1d	1w
Yes	**Mean**	80.00	63.57	35.36	15.71	86.43	72.86	55.00	33.93
(N=14)	**S.D.**	12.86	19.65	24.30	12.07	9.29	22.68	21.12	15.71
No	**Mean**	87.50	80.00	42.50	13.75	86.25	81.25	72.50	42.50
(N=4)	**S.D.**	8.66	24.15	21.79	4.79	11.09	6.29	17.08	5.00
	d	0.62	0.80*	0.30	0.18	0.02	0.41	0.86*	0.60

Seizure Activity During Delay Week

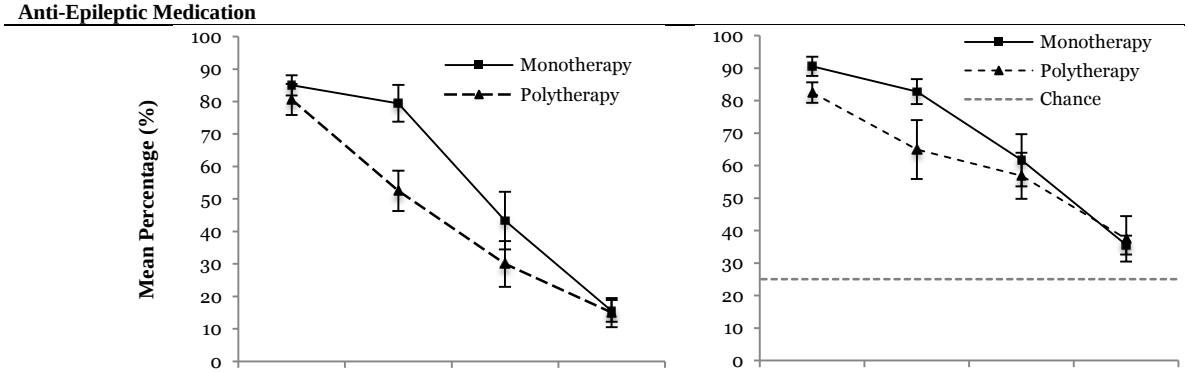




		30s	10m	1d	1w	30s	10m	1d	1w
Yes	**Mean**	80.00	64.00	30.00	12.00	84.00	64.00	51.00	31.00
(N=5)	**S.D.**	16.96	19.81	24.75	11.51	5.48	15.17	28.81	8.94
No	**Mean**	82.31	68.46	39.62	16.54	87.31	78.85	61.92	37.69
(N=13)	**S.D.**	10.73	22.30	23.23	10.68	10.53	21.03	17.97	15.89
	d	0.18	0.21	0.41	0.42	0.35	0.75	0.51	0.46



		Story Task				Route Task			
		30s	10m	1d	1w	30s	10m	1d	1w
Pathology (N=4)	Mean	87.50	46.25	31.25	7.50	81.25	58.75	66.25	37.50
	S.D.	15.55	23.59	24.62	5.00	6.29	23.23	14.93	12.58
Normal (N=12)	Mean	80.83	70.00	36.67	19.17	86.67	79.17	54.58	34.58
	S.D.	12.03	15.67	22.80	10.62	9.85	19.29	22.31	15.88
	d	0.52	1.34*	0.23	1.20*	0.59	1.01*	0.56	0.19



		Story Task				Route Task			
		30s	10m	1d	1w	30s	10m	1d	1w
Monotherapy (N= 9)	Mean	85.00	79.44	43.33	15.56	90.56	82.78	61.67	35.56
	S.D.	9.35	17.04	26.69	10.14	8.82	11.49	23.98	8.82
Polytherapy (N=8)	Mean	80.63	52.50	30.00	15.00	82.50	65.00	56.88	37.50
	S.D.	13.48	17.53	20.00	12.82	8.86	25.63	20.17	19.82
	d	0.38	1.56*	0.56	0.05	0.91*	0.92*	0.21	0.13

*large effect size (d ≥ 0.8)

Figure 6: Sub-Group Long-Term Forgetting Performance on Story and Route Tasks with Descriptive Statistics and Effect Sizes of the Between-Group Difference at Each Delay

4.11.1.5 Age

On the story task, there was a negative trend (alpha between .01 and .05) to significance observed between age and one-week recall, $r(16) = .494$, $p = .037$ (Table 12). This suggested that as age increased one-week story recall decreased. However, when age was entered as a covariate in the 2 (TLE vs CON) x 4 (30s, 10m, 1d, 1w) mixed-model ANOVA, this did not result in a different pattern to that already reported: the between-group interaction remained significant, $F(3,99) = 2.884$, $p = .040$, whilst the interaction with age was non-significant, $F(3,99) = .223$, $p = .880$).

There were no significant correlations between participant age and recall performance on the route task at any delay (Table 13).

4.11.1.6 Age of Onset of Epilepsy

Age of onset of epilepsy did not correlate significantly with recall on either the story or route task at any delay (Tables 12 and 13).

4.11.1.7 Duration of Epilepsy

Duration of epilepsy did not correlate significantly with recall on either the story or route task at any delay (Tables 12 and 13).

4.11.1.8 Mood

There were no significant correlations between mood and recall performance on the story task at any delay (Table 12).

On the route task, at 10-minute delay, there was a significant negative correlation between recall performance and self-reported symptoms of depression, $r(16) = -.619$, $p = .006$ (Table 13). This suggested that as recall performance increased, fewer symptoms of depression were reported. Considering this significant correlation, participants' BDI-II score was entered as a covariate on the previously run 2 (TLE vs CON) x 2 (30s, 10m) mixed-model ANOVA. More variance between 30s and 10m was explained by BDI-II score, $F(1,33) = 9.759$, $p = .004$, than group, $F(1,33) = 1.731$, $p = .197$. Thus, it is possible that lower reported mood influenced accelerated medium-term forgetting to a greater extent than any differences between groups. As participants with TLE reported more symptoms of depression, it is possible experience of depression leads to faster forgetting over this delay or that greater difficulty with memory increases the likelihood of depression.

4.11.2 Variables That May Be Associated With Forgetting Rate

Variables that were highlighted as of interest to explore further regarding their relationship to forgetting, included: intelligence (WASI-II FSIQ-2), performance on standardised memory measures (WMS-III WLI, WLII, VRI and VRII), subjective memory ability (EMQ-R), and subjective spatial navigation ability (SBSOD).

4.11.2.1 Story Task

On the story task, 10-minute recall performance was associated with significant positive correlations (alpha of .01) with intelligence, $r(16) = .694$, p = .001, and delayed verbal memory, $r(16) = .643$, p = .004. This suggested that as recall on the story task at 10-minutes increased, intelligence and delayed verbal memory performance on the standardised memory measure also increased.

No other variables correlated significantly with story recall at any delay (Table 12).

Table 12: Correlation Analyses on the Story Task

	Mean 30-Second Recall		Mean 10-Minute Recall		Mean One-Day Recall		Mean One-Week Recall	
	r	**p**	***r***	**p**	***r***	**p**	***r***	**p**
Age	-.025		.071		-.047		-.494	.037^
Age of Onset	-.174		.412		.210		-.156	
Duration	.157		-.359		-.266		0.332	
WASI-II	.202		.694	.001*	.398		.170	
WMS-III WLI	.023		.517	.028^	.403		.363	
WMS-III WLII	.172		.643	.004*	.340		.063	
EMQ-R	-.380		-.390		-.190		-.232	
BDI-II	-.393		-.385		-.165		.063	
BAI	-.077		-.224		.045		.031	

*significant at .01; ^ 'trend' to significance at .05

4.11.2.2 Route Task

On the route task, 30-second recall performance was associated with significant positive correlations (alpha of .01) with immediate visual memory, $r(16) = .001$. 10-minute recall performance correlated significantly with intelligence, $r(16) = .602$, p = .008, and delayed visual memory, $r(16) = .733$, p = .001. This suggested that as recall on the route task at 10-minutes increased, intelligence and delayed visual memory performance on the standardised memory measure also increased.

Also at 10-minute delay, there were significant negative correlations between route recall performance and subjective everyday memory problems, $r(16) = -.748$, $p < .001$. This suggested that as recall performance decreased, more everyday memory problems were reported. One-day recall performance correlated

significantly with delayed visual memory, $r(16) = .683$, $p = .002$. No other variables significantly correlated with route recall, although there were a number of variables that exhibited a trend to significance (Table 13).

Table 13: Correlation Analyses on the Route Task

	Mean 30-Second Recall		Mean 10-Minute Recall		Mean One-Day Recall		Mean One-Week Recall	
	r	**p**	***r***	**p**	***r***	**p**	***r***	**p**
Age	-.105		.191		.210		-.013	
Age of Onset	.121		.318		.162		.140	
Duration	-.231		-.142		.041		-.159	
WASI-II	.497	.036^	.602	.008*	.504	.033^	.065	
WMS-III VRI	.731	.001*	.533	.023^	.506	.032^	-.033	
WMS-III VRII	.574	.013^	.733	.001*	.683	.002*	.103	
EMQ-R	-.398		-.748	<.001*	-.344		.108	
SBSOD	.401		.513	.030^	.419		.251	
BDI-II	.037		-.619	.006*	-.325		-.011	
BAI	-.219		-.472	.048^	-.026		.102	

*significant at .01; ^ 'trend' to significance at .05

4.11.3 Associations Between Other Variables

Exploring correlations between the questionnaire measures and neuropsychological variables, there was a trend towards significance between subjective memory (EMQ-R) and mood measures (BDI-II and BAI). As self-report of everyday memory problems increased both self-reported symptoms of depression increased, $r(16) = .581$, $p = .012$, and self-reported symptoms of anxiety increased, $r(16) = .525$, $p = .025$.

There was also a trend for significance between subjective memory (EMQ-R) and performance on standardised verbal and visual measures. As self-report of everyday memory problems increased, performance at both immediate and delayed verbal memory decreased, $r(16) = -.554$, $p = .017$, and $r(16) = -.501$, $p = .034$ respectively. The same relationship was observed for immediate visual memory, $r(16) = -.540$, $p = .021$, and a significant relationship was observed for delayed visual memory, $r(16) = -.602$, $p = .008$. Similarly, there was a trend for significance between subjective spatial navigation abilities and performance at immediate visual memory, $r(16) = .477$, $p = .045$.

5. Discussion

This final section summarises the main findings of the study and links these findings to the published literature on long-term forgetting. The methodology of the current study will then be discussed, including its methodological strengths and limitations. The implications, both theoretical and clinical, of the current findings will also be considered and recommendations for future research will be suggested. Finally, the overall conclusions of the study will be presented.

5.1 Summary of Findings

This study aimed to develop two novel measures, a story and a route task, in verbal and visuo-spatial domains with which to assess long-term forgetting that met a number of methodological criteria. To minimise the repeated recall of material at each delay interval the final measures each consisted of four parallel trials with established equivalency of difficulty. The measures were also evidenced to avoid ceiling effects at the initial learning delay and floor effects at the last learning delay in both groups of participants.

These measures were also used to assess for the presence of accelerated long-term forgetting in a sample of participants with TLE compared to neurologically healthy controls. Demographic and neuropsychological profiles of the participants with TLE were comparable to the controls. The groups were matched with regard to age, education, and intelligence. There were additionally no differences between groups on neuropsychological variables, which included immediate and delayed verbal and visual memory. There were, however, a small sub-set of participants with TLE who performed within the 'borderline' to 'impaired' ranges at delayed recall on standardised memory measures, suggesting some evidence of memory deficit on clinically used neuropsychological measures. Participants with TLE additionally reported significantly more symptoms of depression than controls, more problems with their everyday memory, and poorer spatial navigational abilities.

More participants with TLE (albeit the minority) required multiple presentations in both the story and route tasks to reach learning criteria but this matching

procedure succeeded in establishing matched performance between groups at the initial learning delay trial of 30-seconds. With regards to the story task, there was a significant delay-by-group interaction, which showed that participants with TLE forgot the verbal material at an accelerated rate by one-week delay. In contrast, on the route task there was not a significant delay-by-group interaction when examining forgetting over a week period. The participants with TLE, however, forgot this visuo-spatial material at an accelerated rate over the medium-term, 10-minute delay. Rate of forgetting was then comparable between groups over the long-term delays. It is possible this finding of accelerated medium-term forgetting could be explained by variance in mood. Even so, interpretation of this possibility must be cautious due to lack of further correlations between mood and recall at other recall delays.

Although any conclusions made from the exploratory analyses must be tentative due to their reduced power and therefore limited statistical significance, a number of interesting associations were observed. Poorer medium-term recall on the story task was associated with presence of MTL pathology, polytherapy treatment for epilepsy, and to a lesser extent, seizure activity over the past six months. However, only MTL pathology was also somewhat associated with long-term story recall between one-day and one-week delay. There was additionally a trend towards a relationship between age and long-term recall at one-week delay, although further analyses did not implicate age in accelerated forgetting up to one-week.

Poorer medium-term recall on the route task was associated with presence of MTL pathology and polytherapy treatment for epilepsy. To a lesser extent, seizure activity over the past six months was associated with recall at one-day delay. The only variable that was associated with long-term (i.e. one-week) recall was laterality of seizure focus whereby participants with right-hemisphere lateralisation exhibited poorer one-week recall of route material compared with participants with left-hemisphere lateralisation, despite comparable forgetting rates at other delays.

There were a number of significant correlations found between the measures developed and participants' with TLE performance on standardised

neuropsychological measures. On the story task, there were significant relationships between 10-minute story recall, intelligence and delayed verbal memory on standardised measures. On the route task, there were significant correlations with 30-second route recall and immediate visual memory; and 10-minute route recall, intelligence and delayed visual memory on standardised measures.

On other measures, there was a positive trend between number of subjective everyday memory problems and mood measures, with more reported memory problems associated with more symptoms of depression and anxiety. Self-reported memory problems also correlated negatively with performance on standardised verbal and visual memory measures, both at immediate and delayed recall. There was also a positive trend between self-reported spatial navigation abilities and immediate visual memory, where better perceived spatial navigation ability was associated with better performance on immediate visual memory.

5.2 Findings in Relation to the Previous Literature

5.2.1 Story Task

The current study supported the findings in the literature that has suggested that people with TLE forget verbal information at an accelerated rate and that this occurs at long-term delays, lending support to Hypothesis 1(b). However, whilst the current study found no significant difference between groups up to one-day, the one other group study that used the same long-term delays as used presently found that accelerated forgetting occurred most rapidly over the first day, with similar rates of forgetting thereafter (Mulhert et al., 2010). Examining the case study literature, the current findings support those of Lucchelli and Spinnler (1998), who found comparable performance between their case and age- and education-matched controls at one-day but accelerated forgetting by one-week. Other case studies that have found accelerated long-term forgetting after one-day have methodological flaws and floor effects, making conclusions difficult to interpret (i.e. Jansari et al, 2010; O'Connor et al, 1997).

Considering possible reasons why the current study found contrasting results to Mulhert et al.'s (2010) it is worth examining the differences in demographics and methodologies between studies. Sample differences included: the participants were considerably older (mean age 68 versus 39 years); they were diagnosed with TEA rather than TLE; most did not have pathology on MRI; all had been seizure free for at least four months; and no participant had a seizure during the delay. Methodological differences included: control participants were recruited from friends and family of the participant with TEA; they used a word-list task; and repeated recall at each delay. Thus, there may be multiple reasons for the discrepant findings, including: (i) age; (ii) diagnosis; (iii) epilepsy variables; (iv) materials used; (v) nature of controls recruited; and (vi) method of retrieval. All these factors have been found to be associated with forgetting to various degrees (e.g. Kopelman & Stanhope; 1997; Mulhert et al., 2010; Elliott, Isaac & Mulhert, 2014) thus it is likely they influenced the differences of forgetting rate profile found between their study and that found currently.

The only group study (Evans et al., 2014) that used parallel story forms to also minimise repeated recall at each delay trial also found that participants with TLE (who had not undergone neurosurgery) forgot story information at an accelerated rate between immediate learning and one-week delay. However, they did not report non-repeated story recall between these two points, neither at a medium-term nor earlier long-term delay, and so whether they would have found an effect earlier is unclear. With this background, the current study can significantly contribute to the field.

In relation to other exploratory variables and their tentative association with forgetting, accelerated medium-term forgetting was associated most notably with MTL pathology and polytherapy treatment for epilepsy. In other forgetting rate studies, MTL pathology has also been implicated in more rapid forgetting over initial acquisition and retention delays (Butler et al., 2009; Wilkinson et al., 2012). However, in the current study there was additionally a possible relationship between MTL pathology and accelerated forgetting at long-term delays. Although this contrasts the findings of Butler et al. (2009), it supports findings of other research (Mulhert et al., 2011; Wilkinson et al., 2012). Exploration of the

timeframe of MTL involvement in forgetting currently suggested MTL pathology may accelerate forgetting across not only medium-term delays during early retention but also across long-term delays from one-day to one-week post-learning. The finding that polytherapy treatment affected forgetting most notably over medium-term and not over long-term delay has been supported by other findings in the literature (Motamedi & Meador, 2004; Jokeit et al., 2005; Jansari et al., 2010; Midorikawa & Kawamura, 2007).

Lack of lateralisation between participants with left- and right-hemisphere seizure origin has been observed in other studies of long-term forgetting (Martin et al., 1991; Mulhert et al., 2011) but is at odds with other research (Blake et al., 2000; Wilkinson et al., 2012; Jokeit et al., 2001). Currently, there was some tentative suggestion that active seizure activity accelerated medium-term but not long-term forgetting. This finding that seizure activity was not associated with long-term forgetting is supported by other research (Bergin et al., 1995; Fitzgerald et al., 2013b).

5.2.2 Route Task

The current study found that, rather than accelerated forgetting at long-term delays, participants with TLE forgot visuo-spatial material most rapidly over the first 10-minute delay, lending support to Hypothesis 2(a). This finding contrasts with that of Tramoni et al. (2011), the only other study in the literature that used a similar route task to assess long-term forgetting. Whilst in Tramoni's study, participants with TLE exhibited similar performance to controls at one-hour delay they exhibited accelerated forgetting between this trial and six-week delay. Possible reasons for the difference between findings were examined. The sample size in Tramoni's study was small with only five participants with TLE, they were all seizure free, did not have pathology on CT, and they had a mean FSIQ within the 'high average' range. Additionally, they did not match the patient and control groups for intelligence and their measure differed in that they assessed only spatial directions. Performance was also high at 30-minute delay in both groups (in fact at ceiling on the recognition method of retrieval) suggesting the material may have been overlearned during learning, which could have masked forgetting over this first delay trial. Thus, the contradictory findings between this study and

the current one could be explained by methodological differences or be reflective of differences between participant characteristics.

Evidence of accelerated long-term forgetting for visual material in the literature has typically been mixed. Comparing the current results to studies that used a visual task with a spatial element to investigate long-term forgetting (i.e. Davidson et al., 2007; Evans et al., 2014; Mulhert et al., 2011; Narayanan et al., 2012), the current finding that accelerated long-term forgetting did not occur for visuo-spatial material was mostly supported. The exception to this was the study conducted by Evans et al. (2014) that found accelerated long-term forgetting of recall for spatial material beyond the 30-minute delay to one-week. Of note, none of the other three studies found evidence of accelerated forgetting at any delay. Even so, the current finding supports those of past lesion studies that found accelerated forgetting over relatively brief timeframes (Kopelman & Stanhope, 1997; Green & Kopelman, 2002; Isaac & Mayes, 1999a, 1999b). It is possible characteristics of the current sample with TLE led to the finding of accelerated medium-term forgetting, particularly considering their significantly worse ratings of spatial navigation abilities on the SBSOD compared to controls. There has been some suggestion in the wider TLE literature that some people with TLE exhibit difficulties with spatial navigation (Amlerova et al., 2012), which may be indicated in the current sample considering their poorer self-reported navigation abilities.

The relationship between, and possible influence of, lower reported mood and accelerated medium-term forgetting is interesting. Other forgetting studies have not found an association between forgetting and mood in epilepsy populations (Blake et al., 2000; Butler et al., 2007; Mameniskiene et al., 2006; Mulhert et al., 2011) nor has research investigating forgetting in other populations, including those who have a diagnosis of depression (Lewis & Kopelman, 1998; Squire, 1981; Hart, Kwentus, Taylor & Harkins, 1987). Thus, it is possible the current findings are reflective of an artefact in the data. However, it remains a possibility that experience of low mood may be a potential confound that influenced medium-term forgetting rates and is discussed further below.

Similarly to the associations found on the story task at medium-term recall, accelerated medium-term forgetting on the route task was also tentatively associated with MTL pathology and polytherapy treatment for epilepsy. As discussed earlier, these findings support research that has suggested MTL pathology, and greater numbers of AEDs, are implicated in early retention of material but are less implicated at longer-term delays (Butler et al., 2009; Wilkinson et al., 2012; Motamedi & Meador, 2004; Jokeit et al., 2005; Lee, 2010). Even so, MTL pathology was less strongly associated on the route compared to the story task at long-term delay currently. This mixed finding between verbal and visual task results has been found in other studies in the literature (e.g. Wilkinson et al., 2012) and currently may be reflective of the sample recruited. Only one participant out of the four with pathology on MRI had mesial temporal sclerosis lateralised in the right temporal lobe, thus if lateralisation of pathology is additionally involved in forgetting at long-term delays it is unlikely this would have been observed currently. The group with MTL pathology also exhibited an atypical forgetting curve, whereby their performance improved between 10-minute and one-day recall, which may have masked any differences in forgetting rate.

Lateralisation of seizure focus was currently found to be the only variable that was associated with long-term forgetting of the route material. Those with right-hemisphere laterality exhibited poorer recall at one-week delay despite comparable forgetting rates before this. Some studies have found a similar trend towards accelerated long-term forgetting in participants with right-sided seizure focus (Wilkinson et al., 2012; Narayanan et al., 2012) but this finding is variable (Martin et al., 1991; Mulhert et al., 2011).

5.2.3 Other Exploratory Analyses

Currently, self-report of poorer everyday memory correlated with mood and standardised memory measures. This finding that reports of poor subjective memory is related to low mood has been corroborated by other research in the forgetting literature (Mulhert et al., 2011; Hall, Isaac & Harris, 2009; Elixhauser et al., 1999).

5.3 Methodological Issues

5.3.1 Strengths

5.3.1.1 Methodological Criteria

The current study aimed to develop two novel measures that met a number of methodological criteria with the aim of minimising methodological flaws of previous research. These measures succeeded in meeting these aims considering they: (i) minimised repeated recall of the same material through the use of parallel forms of established equivalency; (ii) avoided ceiling effects at the first recall delay; (iii) avoided floor effects at the last recall delay; and (iv) successfully matched groups for age, education, intelligence, and level of initial learning.

Elliott et al. (2014) have recently published a methodological critique of the accelerated long-term forgetting in epilepsy literature. They posited a number of recommendations to follow in the design of such studies, including: (i) to match patient and control groups for age and intelligence; (ii) to use both verbal and non-verbal test material; (iii) to use recall and recognition tests for each measure; (iv) to avoid ceiling and floor effects; (v) to avoid rehearsal and repeated recall; (vi) to use an immediate delay period that is not boosted by short-term memory; and (vii) to equate initial learning whilst avoiding overlearning. Based on these recommendations, it is clear the only criteria the current study methodology did not meet was to use both recall and recognition tests for each measure. This will be considered further below. However, of the 21 group studies they compared to these recommendations, only two met most of these recommendations (Mulhert et al., 2011; Evans et al., 2014). Thus, it is evident that there is a scarcity in the literature for well-designed studies in this area and the current study fulfils the majority of these methodological considerations.

5.3.1.2 Validity of Forgetting Measures

Additionally, the measures developed displayed concurrent validity with other standardised memory measures at the medium-term delay of 10-minutes. Recall on the story task at 10-minutes correlated significantly with delayed verbal recall and recall on the route task at 10-minutes correlated significantly with delayed

visual recall. Both measures also correlated significantly with intelligence at this delay, which has been found to be related to memory performance on standardised instruments at similar delays (Groth-Marnat, 2003). Thus, this suggests the current measures developed employed similar constructs to those of well-established memory measures.

5.3.1.3 Feasibility of Remote Long-Term Follow-Up

The current study was also one of the few studies that attempted to assess long-term recall over the phone. Using this method to assess recall for verbal material was overall found to be incredibly practicable. This method is likely to have increased the rate of recruitment and ensured data points were not missed: testing at convenient times (e.g. outside of work hours) could be made with participants to conduct follow-up phone calls. This method has also been found to be feasible in other studies on long-term forgetting (Baddeley et al., 2013; Kemp et al., 2012). The current study additionally attempted to assess long-term recall of visuo-spatial route material over the phone, which has not been attempted in previous research using a similar task. Again, the use of email to send password-protected pdf picture files and giving directions over the phone for participants' using these files to assess spatial decision recognition at long-term delays proved successful. There is an identified need in the literature to develop practical tools with which to assess long-term forgetting (Elliott et al., 2014; Baddeley et al., 2013); thus the current initial development of tools to assess long-term visuo-spatial material shows the feasibility of using similar methods to assess long-term recall in the future.

5.3.2 Limitations

5.3.2.1 Sample Size

The first limitation of the study was its limited capability to detect small- or medium- sized effects. Although more participants were recruited than targeted based on the power analysis calculation, the study still only had sufficient power to detect large effects and it is likely that some important effects were not statistically significant because of this. For example, on visual inspection of the graph plotting forgetting rates on the story task it is clear that the groups began diverging from each other by one-day delay but the effect size was of only a medium size. Thus,

studies that found most forgetting by one-day delay may have simply had more power to detect a smaller difference between groups. Revisiting the group studies that found significant accelerated forgetting by this delay there is a possibility this may be the case. Although it was not possible to calculate effect sizes for all of these studies, their sample sizes were generally larger than that currently, ranging from 42 to 68 participants in total (Bengner et al., 2006; Fitzgerald et al., 2013b; Martin et al., 1991). However, two studies that found significant effects after one-day had a smaller sample size than that currently (Jokeit et al., 2001; Mulhert et al., 2010). Even so, as discussed previously Mulhert et al. (2010) found much larger effect sizes between their groups and there were a number of differences between methodologies, suggesting this may not be the most appropriate comparison. It would be valuable for future research to develop a greater understanding of the power different long-term forgetting studies had to detect significantly different effects, which may go some way to explain the reported differences in timeframe of accelerated forgetting found between studies.

Similarly, sufficient power to detect a significant difference was only calculated based on the primary hypotheses. Therefore, although the other variables explored in further analyses are likely to have played a varying role in accelerated forgetting rates (particularly those with large effect sizes), the smaller sample size of each sub-group meant that the power to detect a significant difference was unlikely. Even so, it is worth noting that despite this, interactions between sub-groups approached significance in some instances (e.g. between medium-term forgetting on the story task, MTL pathology and polytherapy treatment). Thus, although these exploratory analyses must be tentative, they still highlight possible variables that are important to explore or control for in forgetting studies.

5.3.2.2 Sample Characteristics

Other research investigating long-term forgetting in epilepsy has controlled characteristics of the sample to varying degrees. For example, some have ensured the entire sample is free of seizures and on monotherapy treatment (e.g. Mulhert et al., 2010), some have only included participants with no pathology on neuroimaging (e.g. Tramoni et al., 2011), whilst others have only recruited participants with confirmed laterality of seizure focus (e.g. Wilkinson et al., 2012).

However, stringent control of possibly influential epilepsy variables was beyond the scope of the current study and so it was decided to be more appropriate to simply examine the possible influence of these variables, despite the limitations of this approach (described above).

Although the current study was successful in matching participants on measures that have been highlighted by the literature as important to control (age, education, and intelligence), and additionally matched participants on other measures of cognition, the groups did differ on measures of mood, albeit not at clinically concerning levels. Despite previous literature suggesting mood does not influence forgetting rates, mood score currently was related to findings of accelerated medium-term forgetting on the route task. Although this may be a spurious result as mood was not associated with forgetting on the story task or performance at other delays on the route task, it is also possible participants' mood influenced medium-term forgetting rates more than group categorisation. If this was the case, it would suggest participants with TLE did not forget route material at an accelerated rate at this medium-term delay (and therein did not exhibit any evidence of accelerated forgetting on this task). Therefore, it would have been beneficial for the current study if the groups had been additionally matched for mood score to minimise the possibility that low mood confounded recall performance. Even so, considering psychiatric co-morbidity was an exclusion criterion in the screening process for eligible participants presently it had been anticipated that there would not be a between-group difference in mood. If it is the case that experience of depression is more prevalent in this population (as has been evidenced in, for example, Butterbaugh et al., 2005; Bragatti et al., 2011), future research may need to recruit control participants from a sample with similar levels of low mood to control for this in future.

5.3.2.3 Measurement

Elliott et al. (2014) recommended that long-term forgetting studies assess memory through both recall and recognition methods. These methods of retrieval have been found to result in different forgetting rates (Kopelman & Stanhope, 1997; Green & Kopelman, 2002; Isaac & Mayes, 1999a, 1999b; Freed & Corkin, 1988). Thus, using multiple methods of retrieval at long-term intervals allows for

extrapolation of what aspects of memory may be relatively compromised if accelerated forgetting for one, or more, retrieval method is found. Currently, only a cued recall method of memory retrieval was utilised on the story task, therefore it was not possible to ascertain whether participants could have recollected material when provided a choice of options. Even so, cued recall has been suggested to be more sensitive than recognition tests and allows for more control over retrieval than free recall (Baddeley et al., 2013). Similarly, recognition memory has generally found to not be implicated in forgetting studies (Kopelman & Stanhope, 1997; Green & Kopelman, 2002; Butler & Zeman, 2008b). Even so, using a recognition memory procedure as part of the story task would have increased its methodological strength.

In contrast, although the route task did utilise both recognition and cued recall procedures, it was analysed as a composite score considering there were only five items that made up each retrieval method. Due to the small range of observations at each time point when this task was separated and the influence of chance performance considering the forced-choice nature of the recognition task, analysing route memory as two separate constructs would have limited its sensitivity to detect a difference. However, as recall and recognition can result in different forgetting rates, as described above, this approach had clear limitations. In future, further development of this task would be desirable to include a greater number of data points for the recognition and cued recall methods of retrieval at each delay trial to allow analysis of retrieval method at different delay points.

In relation to conducting long-term recall trials over the telephone, there are some limitations noted with this approach. More detailed recall testing was not possible and visuo-spatial recall had to be verbalised, thus it could be argued that the route task was not a pure measure of visuo-spatial ability (Narayanan et al., 2012). Additionally, informing participants of, and organising, telephone calls during the research interview may have prompted some to rehearse material during the delay period. However, participants were instructed not to rehearse during the delay and when questioned all participants denied rehearsal. No participant's long-term recall performance appeared disproportionate to their performance during the research assessment, indicating it was unlikely that this was an issue.

5.4 Implications of Findings

5.4.1 Theoretical Implications

5.4.1.1 Acquisition Versus Consolidation Deficit

Considering a third of participants with TLE required multiple presentations of the story task and a sixth required multiple presentation of the route task to establish matched performance to control participants at 30-second delay, it is likely that at least some participants with TLE exhibited a difficulty in the acquisition of new material. Experimental manipulation with regards to matching at this delay attempted to enhance levels of encoding but it is possible secondary retrieval deficits associated with relatively poorer acquisition affected recall at later delays in these participants (Green & Kopelman, 2002).

On the route task, participants with TLE forgot material most rapidly between the first two delay points, i.e. between 30-second and 10-minute delays, with comparable forgetting rates thereafter. Additionally, some sub-groups within the TLE sample seemingly forgot both verbal and visuo-spatial material most rapidly by 10-minute delay. This finding lends support to the suggestion that after matching for differences in short-term memory during initial learning, there may be an additional deficit in retention observed between groups: but that this is detectable over a relatively short timeframe and likely corresponds to disruption to fairly early stages of memory consolidation. This, again, lends support to past accelerated forgetting studies that found evidence of deficits in retention by similar intervals (Green & Kopelman, 2002; Kopelman & Stanhope, 1997; Isaac & Mayes, 1999a).

Conversely, on the story task, accelerated forgetting was not evident amongst the participants with TLE until one-week delay. This could suggest that there was disruption to secondary consolidation processes that are distinct from processes involved in the initial consolidation of memories. This view has been advocated by many researchers in this field (e.g. Butler et al., 2010; Elliott et al., 2014). However, whether this finding is in fact a subtle deficit during early consolidation that becomes more pronounced over time is currently unknown. Certainly in the

current study, a small effect was noted between groups at 10-minute delay, which became a medium effect by one-day delay, and a large effect by one-week delay. It is possible other studies also demonstrate a similar forgetting curve and have been likewise limited by their power to detect a difference before long-term testing intervals.

Revisiting the past group studies listed in Table 1, in only two studies (Tramoni et al., 2011; Gascoigne et al., 2012) were the patient groups' performance on all measures at the medium-term delay similar to the control groups'. In all other studies the patient groups' performance at this delay was lower than the control groups', sometimes to a similar (subtle) degree as that found currently, but sometimes significantly lower (e.g. Helmstaedter et al., 1998; Bell, 2006; Mameniskiene et al., 2006; Butler et al., 2007; Djordjevic et al., 2011; Narayanan et al., 2012). Thus, the possibility remains that a subtle disruption to early stages of memory consolidation results in increasingly pronounced accelerated forgetting at long delays, rather than accelerated forgetting only occurring after secondary consolidation processes are disrupted, which may not occur for days or weeks. Future work that could elucidate understanding to this question is described further below.

5.4.1.2 Comparison to Theories of Memory Consolidation

The results from the story task currently showed that any difference between groups at 10-minute delay was subtle and that as time increased the rate of forgetting also increased. This finding, therefore, adds to the literature refuting the premise of Atkinson and Shiffrin's (1968) model that memories enter a long-term store and become robust to forgetting fairly rapidly, i.e. over medium-term recall delays currently. Instead, forgetting appeared to continue over a much longer time scale.

Additionally, the tentative finding that participants with TLE with MTL pathology exhibited more rapid medium-term forgetting provides support for the theories of memory consolidation (both the 'standard model' and 'multiple trace theory') that postulate encoding and initial consolidation of memory traces are dependent on MTL structures. The additional finding that MTL pathology was also possibly

implicated in long-term forgetting on the story task may provide further support for the 'multiple trace theory' premise that memories remain dependent on MTL structures even beyond initial, rapid, consolidation. However, the 'standard theory' does not posit the timeframe over which memories become independent of the MTL and considering this analysis in the current study was based on a small sub-group of the participants, which was not the primary aim of the study, support for or against the different theories of memory consolidation cannot be comprehensively addressed presently.

5.4.2 Clinical Implications

5.4.2.1 Assessment

The primary findings of the current study suggested that participants with TLE exhibited accelerated long-term forgetting on a story task over a delay of one-week despite fairly similar performance to control participants on the story task at medium-term delay and no evidence at the group level of cognitive impairment on standardised neuropsychological tests. Although a sub-set of participants with TLE demonstrated 'impaired' performance on these standardised measures, the majority performed within 'normal' ranges despite significantly more participants with TLE complaining of memory problems in their everyday life. These discrepancies highlight the limitations of memory assessment measures used currently in clinical settings. Considering other studies have also noted such differences, it is likely that a fair proportion of people with TLE who self-report memory difficulties yet perform within 'normal' ranges on standardised memory tests do have an organic problem that is being undetected currently. Even if it is the case that people with TLE experience subtle difficulties in memory acquisition or deficits during early consolidation processes, clinical measures are not currently sensitive enough to detect these differences, and disparities in performance seem to only become apparent by longer delays.

Lack of recognition of this problem in clinic settings may increase patients' feelings of frustration, impact their everyday functioning and affect relationships through lack of understanding of an organic memory problem. Simply becoming aware of and normalising the presence of accelerated forgetting may be of clinical utility.

Therefore, there is a clinical need to develop methods with which to measure memory recall at longer-term delays, beyond the clinical assessment session, when a person presents in clinical settings with memory complaints indicative of accelerated forgetting, as recommended by Witt et al. (2012). Currently, the ease of measuring long-term recall by telephone proved highly practicable and could easily be incorporated in clinical practice as a patient-friendly and convenient way to assess recall at these longer-term delays. Thus, the measures developed for the current study may be of value (albeit with the need for further modifications) in the preliminary establishment of methodologically valid clinical tools to assess long-term forgetting.

In relation to the visuo-spatial task, the discrepancy between comparable delayed visual memory performance on the standardised memory measure between groups yet evidence of accelerated medium-term forgetting on the experimental route task may indicate a greater need to assess visuo-spatial ability in clinical settings. Considering it has been suggested that people with TLE exhibit spatial memory difficulties this may be particularly pertinent (Amlerova et al., 2012).

5.4.2.2 Rehabilitation

Although the premise of the current study was not to investigate methods to ameliorate accelerated forgetting, a number of findings may highlight factors that, if not optimally controlled, could influence forgetting rates. Medium-term forgetting on both the story and route tasks currently was associated with polytherapy treatment for epilepsy, thus regular reviews of optimal medication doses and, in cases where polytherapy is indicated, consideration of the consequences on memory (and sign-posting to services who may aid with compensatory strategies) is recommended. Additionally, in the current study presence of low mood was also implicated in accelerated medium-term forgetting on the route task. Considering more participants with TLE scored within 'moderate' to 'severe' ranges on the depression scale than controls, despite there being an exclusion criteria regarding psychiatric co-morbidity, this perhaps indicates that experience of depression is more prevalent in the TLE population and is not being adequately screened for and assessed in clinical settings presently (O'Donoghue, Goodridge, Redhead, Sander & Duncan, 1999; Wiegartz, Seidenberg,

Woodard, Gidal & Hermann, 1999). This highlights the need for epilepsy clinics to assess and, where appropriate, refer patients with mood problems for treatment, which may consequently improve their performance on memory measures.

Although epilepsy management procedures have also been postulated to improve long-term forgetting rates as a secondary consequence (Evans et al., 2014; Gallassi et al., 2011), it may be that memory strategy training and advice to enhance encoding and improve rates of accelerated forgetting could also be of clinical utility (Jansari et al., 2010; McGibbon & Jansari, 2013). Further research investigating the efficacy of both internal and compensatory memory strategies in the amelioration of accelerated forgetting in this population is therefore warranted.

5.5 Future Directions

In the current study, groups were matched for initial learning at 30-second delay, as has been recommended by Elliott et al. (2014). However, some studies examining accelerated forgetting in lesion groups matched groups for performance at 10-minute delay (Huppert & Piercy, 1978; 1979). Although matching performance at this delay was important in these studies due to the more 'classic' presentations of amnesia in lesion populations, which is less commonly observed in people with TLE, it still raises the question of which delay to match performance to. This is particularly pertinent considering the proposition that accelerated 'long-term' forgetting in this population may be a consequence of subtle disruption to early consolidation processes that becomes more pronounced over time. Therefore, analysis of long-term forgetting rates would have been more informative had performance been similar between groups at medium-term delay. Thus, it may be beneficial in future research to match, or exaggerate, an individual's performance during initial learning to ensure that performance at the first medium-term delay is then comparable. If accelerated forgetting is still observed to occur over longer delays following this matching, this would indicate that disruption to secondary consolidation processes do play a role in the observation of this phenomenon.

On a related note, much of the research in this area has measured recall at a delay of about 30 minutes and then again at one or more long-term delays (between one-

day and eight-weeks). However, it is possible accelerated forgetting occurs over a much shorter timeframe than investigated (Kopelman & Stanhope, 1997; Green & Kopelman, 2002; Isaac & Mayes, 1999a, 1999b). This question has been examined in only one case study. McGibbon and Jansari (2013) showed that in a patient with TLE, who they had previously claimed exhibited accelerated long-term forgetting over a 24-hour delay (Jansari et al., 2010) actually demonstrated most rapid forgetting over 55-minutes. Thus, it is possible in the studies that found most forgetting at the first long-term delay they may have found most rapid forgetting before this delay trial and that 'long-term' forgetting actually occurs over a much briefer timeframe. Future research utilising delay trials at hours post-learning rather than days will be able to investigate this hypothesis at a group level.

Currently, the only epilepsy variables found to be tentatively implicated in accelerated long-term forgetting were presence of MTL pathology (on the story task) and laterality of seizure focus (on the route task). However, it is possible that different long-term forgetting rates would have been found had participants in the current study also included those with lateral TLE. Investigation of how memories are consolidated within different systems in the temporal lobes and the timeframe over which consolidation occurs is still on-going and so comparing forgetting rates between groups with mesial TLE versus lateral TLE may further develop understanding of systems processes occurring.

5.6 Summary and Conclusions

People with TLE frequently complain of memory problems despite often performing within 'normal' ranges of memory performance on standardised neuropsychological tests. Some have suggested this discrepancy may be because people with TLE are able to acquire and retain material sufficiently during initial consolidation, which is adequately assessed with current neuropsychological measures, but that factors associated with their epilepsy consequently disrupt secondary memory consolidation processes, which occurs across a longer timeframe than initial consolidation. This disruption to secondary consolidation may result in accelerated long-term forgetting. There is an expanding evidence base that suggests this phenomenon does occur in this population but there are very few studies in the literature that have been methodologically robust. This,

therefore, raises the question of whether this phenomenon would still be observed when methodological confounds have been controlled for.

The current study investigated whether accelerated long-term forgetting was still present in this population after careful consideration of the design to meet a number of methodological criteria. The study succeeded in its aims of designing two novel measures, a verbal story and a visuo-spatial route task, that minimised repeated recall of material, avoided ceiling and floor effects, and matched levels of initial learning between groups whilst avoiding overlearning. The TLE group was also successfully matched to a neurologically healthy control sample on age, education and IQ variables.

Evidence of accelerated forgetting was found on both verbal and visuo-spatial tasks. Accelerated forgetting on the route task occurred over the medium-term delay between 30-seconds and 10-minutes, whilst accelerated forgetting on the story task occurred over the long-term delay, i.e. by one-week. Why these differences were found in relation to when most rapid forgetting occurred is not clear. Previous studies, however, have also found inconsistencies between verbal and visual forgetting tasks and currently there may have been an influence of mood affecting forgetting at 10-minute delay on the route task.

Exploratory analyses of factors associated with epilepsy and their relationship to forgetting suggested that presence of MTL pathology, laterality of seizure onset, and polytherapy were most commonly associated with forgetting across different delays on both the verbal and visuo-spatial measures (although considering power to detect a significant interaction was limited these conclusions must be cautious). MTL pathology and polytherapy influenced medium-term forgetting on both tasks to varying extents. MTL pathology additionally tentatively influenced long-term forgetting on the story task, whilst laterality of seizure onset influenced long-term forgetting on the route task.

Thus, the current study contributed to the current evidence base in this area with overall findings that accelerated forgetting does occur in the population with TLE even with a methodologically rigorous design. Future work can build on the

current data by: further design of measures that are appropriate to use in long-term forgetting research; the use of larger samples with more control, or experimental manipulation, of variables that may be involved in accelerating forgetting; and further exploration of the timeframe at which accelerated forgetting occurs. A key implication from this study relates to the constraints of standardised measures used in clinical neuropsychological assessment presently. Findings of both accelerated long-term forgetting on the story task and accelerated medium-term forgetting on the route task opens the debate for how to improve standardised measures to assess for subtler, but no less functionally significant, memory problems.

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7. Appendices

Appendix 1: Story Task

Story A

A teenager arrived for a sailing trip in Portsmouth at 12:15. The wind was strong at sea and they sailed too close to another yacht. To avoid crashing, the instructor changed direction, but they hit some rocks and the motor got stuck.

Story B

A 30-year-old researcher at the University of Bristol discovered some bacteria that could treat obesity. She received an award from the Royal Society of Medicine for £50,000. With this money, she started an international study across England and Spain.

Story C

George, a farmer in Northumberland, was woken by thunder. His animals were whining so he went outside with a torch. His chicken coop had been struck by lightning, and five horses had escaped. The next day the villagers helped repair his damaged fences.

Story D

Mrs Janet Spring, a Royal Mail employee, was locked in the post room on Tuesday for two hours. A security guard heard her shouting, but he had lost the keys. He had to call the police who broke down the door.

Cued Recall Questions and Scoring Criteria

Story A				
"Just now / a little while ago / yesterday / last week, you heard a story about a trip". Ask cued recall questions in order.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1	What kind of trip was it?	Sailing	2 1	Sailing, boat Reference to the sea
2	Who arrived for the sailing trip?	Teenager	2 1	Teenager Young person [man, woman]
3	What time did the teenager arrive for the sailing trip?	12:15	2 1	12:15 12:00 – 12:30 or :15 past an hour
4	What town did they sail from?	Portsmouth	2 1	Portsmouth Coastal town beginning in P (e.g. Plymouth)
5	What was the wind like at sea?	Strong	2 1	Strong, rough, very [word to describe windy] Breezy
6	What did they sail too close to?	Another yacht	2	Yacht, boat, ship
7	Who did something to avoid crashing?	Instructor	2	Indication that it was the person in charge i.e. instructor, captain, skipper, teacher
8	What did the instructor do?	Changed direction	2	Changed direction, Turned boat, Steered away
9	What did they hit?	Rocks	2	Rocks
10	What got stuck in the rocks?	Motor	2 1	Motor, engine Rudder, propeller

Story B				
"Just now / a little while ago / yesterday / last week, you heard a story about a discovery". Ask cued recall questions in order.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1	What is the profession of the person who made the discovery?	Researcher	2 1	Researcher Scientist
2	How old is the researcher?	30	2 1	30 +/-5 years
3	What university does she work at?	Bristol	2	Bristol
4	What did she discover?	Bacteria	2	Bacteria
5	What could this bacteria help treat?	Obesity	2	Obesity, fatness
6	What did she receive?	Award	2 1	Award, reward, prize, grant Money
7	Who did she receive the award from?	Royal Society of Medicine	2 1	Royal Society of Medicine, Royal Medical Society [Body of] medicine e.g. institute, council, research
8	How much was her award for?	£50,000	2 1	£50,000 +/- a 0, anything in £…0,000
9	How many countries are in the study she started?	2	2	2
10	What country outside of England is involved in her study?	Spain	2	Spain

Story C				
"Just now / a little while ago / yesterday / last week, you heard a story about a farmer". Ask cued recall questions in order.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1	What is the farmer's name?	George	2	George
2	Where does George live?	Northumberland	2 1	Northumberland Town/area beginning North
3	What was he woken by?	Thunder	2 1	Thunder Storm
4	What did her hear after he'd been woken by thunder?	Animals whining	2 1	Animals whining (any word to describe animals making noise) Specific animal making noise, noise/whining unspecified
5	What did he go outside with?	Torch	2	Torch
6	What had been struck by lightning?	Chicken coop	2	Chicken coop/shed/hut
7	Which of his animals had escaped?	Horses	2	Horses
8	How many horses had escaped?	5	2 1	5 +/- 1
9	Who helped him the next day?	Villagers	2 1	Villagers Neighbours
10	What did the villagers help repair?	Fences	2 1	Fences Gates

Story D				
"Just now / a little while ago / yesterday / last week, you heard a story about Mrs Spring". Ask cued recall questions in order.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1	What is Mrs Spring's first name?	Janet	2 1	Janet Name beginning with J
2	Who does Janet work for?	Royal Mail	2 1	Royal Mail Post Office, mail/postal service
3	Where was Janet locked in?	Post room	2 1	Post room Store room, mail room, parcel room, delivery room
4	What day of the week was she locked in the post room?	Tuesday	2	Tuesday
5	How long was she locked inside for?	2 hours	2	2 hours
6	Who found her?	Security guard	2	Security guard
7	How did the security guard know she was there?	Shouting	2 1	Shouting Another word for shouting: screaming, yelling, calling
8	Why could he not get her out?	Lost keys	2 1	Lost keys Didn't have keys, forgot key
9	Who did he call?	Police	2	Police
10	What did the police do?	Broke down door	2	Broke down door, knocked down door

Appendix 2: Route Task

Orienting Instructions

Route A		
Pause Point	**Time**	**Orienting Instructions**
1	0:06	*"Pay attention to the direction we go here"*
2	0:22	*"Pay attention to the direction we go here and to this landmark"* (point to landmark)
3	0:44	*"Pay attention to the name of this autocentre"* (point to autocentre)
4	0:49	*"Pay attention to the direction we go here"*
5	0:59	*"Pay attention to the direction we go here and to this supermarket"* (point to supermarket)
6	1:13	*"Pay attention to the side of the road this train station is on"* (point to train station)
7	1:25	*"Pay attention to the direction we go here"*
8	1:33	*"Pay attention to the name of this restaurant"* (point to restaurant)

Route B		
Pause Point	**Time**	**Orienting Instructions**
1	0:03	*"Pay attention to the direction we go here"*
2	0:12	*"Pay attention to the kind of shop this is"* (point to estate agents)
3	0:20	*"Pay attention to the direction we go here"*
4	0:40	*"Pay attention to the direction we go here and to the name of this car dealership"* (point to car dealership)
5	1:03	*"Pay attention to the colour of the Davenies school sign"* (point to sign)
6	1:14	*"Pay attention to the direction we go here"*
7	1:31	*"Pay attention to the subject that this national school teaches"* (point to the name of the school)
8	1:40	*"Pay attention to the direction we go here"*
9	1:57	*"Pay attention to the age group this learning centre is for"* (point to learning centre)

Route C

Pause Point	Time	Orienting Instructions
1	0:06	*"Pay attention to the direction we go here"*
2	0:30	*"Pay attention to the name of this bank"* (point to bank)
3	0:36	*"Pay attention to the direction we go here"*
4	1:07	*"Pay attention to the direction we go here and to this supermarket"* (point to supermarket)
5	1:20	*"Pay attention to the direction we go here and to this retail store"* (point to retail store)
6	1:37	*"Pay attention to the direction we go here and to this supermarket's petrol station"* (point to supermarket petrol station)
7	1:51	*"Pay attention to the name of the motorway on this sign"*

Route D

Pause Point	Time	Orienting Instructions
1	0:03	*"Pay attention to the direction we go here"*
2	0:23	*"Pay attention to the type of vehicle on this sign"* (point to the sign)
3	0:30	*"Pay attention to the direction we go here"*
4	0:42	*"Pay attention to the name of this pub"* (point to pub)
5	0:57	*"Pay attention to the direction we go here"*
6	1:11	*"Pay attention to the name of this bank"* (point to bank)
7	1:23	*"Pay attention to the direction we go here"*
8	1:32	*"Pay attention to the name of this hotel"* (point to hotel)
9	1:47	*"Pay attention to the direction we go here"*
10	1:53	*"Pay attention to the dance advertised on this sign"* (point to the sign)

Recall Questions and Scoring Criteria

Route A				
"Just now / a little while ago / yesterday / last week, you watched a video of a car driving through a town." Either open or instruct participant to open pdf file and go to Photo 1A.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1A	Which way did we go here: 1 or 2?	1	2	1
1B	What kind of landmark did we pass after this junction?	Church	2	Church
2A	Which way did we go here: 1 or 2?	1	2	1
2B	What is the name of the autocentre we passed after this junction?	Broadway	2 1	Broadway Described sign (i.e. yellow & blue)
3A	Which way did we go here: 1 or 2?	1	2	1
3B	What is the name of the supermarket we passed after this turning?	Waitrose	2	Waitrose
4A	Which way did we go here: 1 or 2?	2	2	2
4B	What side of the road is the train station on after this roundabout?	Left	2	Left
5A	Which way did we go here: 1 or 2?	1	2	1
5B	What is the name of the restaurant we passed after this roundabout?	China Diner	2 1	China Diner Chinese restaurant

Route B				
"Just now / a little while ago / yesterday / last week, you watched a video of a car driving through a town." Either open or instruct participant to open pdf file and go to Photo 1A.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1A	Which way did we go here: 1 or 2?	2	2	2
1B	What kind of shop did we pass after this roundabout?	Estate agents	2	Estate agents
2A	Which way did we go here: 1 or 2?	1	2	1
2B	What is the name of the car dealership we passed after driving through the car park?	Mercedez-Benz	2	Mercedez-Benx
3A	Which way did we go here: 1 or 2?	2	2	2
3B	What is the colour of the Davenies school sign after this junction?	White	2	White
4A	Which way did we go here: 1 or 2?	2	2	2
4B	What subject does the national school after this junction specialise in?	Film & TV	2	Film *or* TV
5A	Which way did we go here: 1 or 2?	2	2	2
5B	What age group does the learning centre after this junction cater for?	Adults	2	Adults, 18+

Route C				
"Just now / a little while ago / yesterday / last week, you watched a video of a car driving through a town." Either open or instruct participant to open pdf file and go to Photo 1A.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1A	Which way did we go here: 1 or 2?	2	2	2
1B	What is the name of the bank we passed after this junction?	HSBC	2	HSBC
2A	Which way did we go here: 1 or 2?	2	2	2
2B	What is the name of the supermarket we approached after this junction?	Sainsburys	2	Sainsburys
3A	Which way did we go here: 1 or 2?	1	2	1
3B	What is the name of the retail store we passed after this junction?	Matalan	2	Matalan
4A	Which way did we go here: 1 or 2?	2	2	2
4B	What supermarket's petrol station did we pass after this junction?	Morrisons	2	Morrisons
5A	Which way did we go here: 1 or 2?	2	2	2
5B	What is the name of the motorway on the sign after this roundabout?	M40	2 1	M40 M4 or M…0

Route D				
"Just now / a little while ago / yesterday / last week, you watched a video of a car driving through a town." Either open or instruct participant to open pdf file and go to Photo 1A.				
Item	**Recall Question**	**Correct Answer**	**Point**	**Scoring Guideline**
1A	Which way did we go here: 1 or 2?	2	2	2
1B	What type of vehicle was on the sign after this junction?	Lorry	2	Lorry, truck
2A	Which way did we go here: 1 or 2?	1	2	1
2B	What is the name of the pub we passed after this junction?	Yates	2	Yates
3A	Which way did we go here: 1 or 2?	2	2	2
3B	What is the name of the bank we passed after this junction?	Yorkshire	2 1	Yorkshire York
4A	Which way did we go here: 1 or 2?	1	2	1
4B	What is the name of the hotel we passed after this junction?	Travelodge	2	Travelodge
5A	Which way did we go here: 1 or 2?	1	2	1
5B	What kind of dance was advertised on a building after this junction?	Salsa	2	Salsa

Appendix 3: Confirmation of Ethical Approval

NHS
Health Research Authority

NRES Committee London - City & East
Bristol Research Ethics Committee Centre
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 01173421386
Facsimile: 01173420445

21 May 2013

Miss Anneli Cassel
Institute of Psychiatry, Kings College London
4 Windsor Walk
London
SE5 8BB

Dear Miss Cassel

Study title: **Does accelerated long-term forgetting occur in people with temporal lobe epilepsy (TLE), transient epileptic amnesia (TEA) and/or people with medial temporal lobe (MTL) lesions?**
REC reference: **13/LO/0399**
IRAS project ID: **116519**

Thank you for your email of 21 May 2013. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 16 May 2013. I can also confirm that all the conditions of the favourable opinion have now been met.

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Participant Information Sheet - Controls	3	20 May 2013
Participant Information Sheet - Patients	3	20 May 2013

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Advertisement	1.0	15 February 2013
Covering Letter		25 April 2013
Evidence of insurance or indemnity		01 August 2012
GP/Consultant Information Sheets	1.0	15 February 2013

Investigator CV		05 March 2013
Other: CV for supervisor (student research)		
Participant Consent Form - Patients	1.0	15 February 2013
Participant Consent Form - Controls	1.0	15 February 2013
Participant Information Sheet - Controls	3	20 May 2013
Participant Information Sheet - Patients	3	20 May 2013
Protocol	2	19 April 2013
REC application		06 March 2013
Referees or other scientific critique report		30 October 2012
Response to Request for Further Information		25 April 2013

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

13/LO/0399 **Please quote this number on all correspondence**

Yours sincerely

Mr Rajat Khullar
Committee Co-ordinator

E-mail: nrescommittee.london-cityandeast@nhs.net

Copy to: *Jennifer Liebscher, Institute of Psychiatry/South London and Maudsley NHS Foundation Trust*

Appendix 4: Invitation Letter Sent From KCH and GSTT

King's College Hospital NHS
NHS Foundation Trust

Professor Robin Morris

Department of Clinical Neuropsychology
9th Floor, Ruskin Wing
King's College Hospital
Denmark Hill
London SE5 9RS

Tel: 0203 299 8330

<<Date>>

<<Recipient Address>>

Dear <<Recipient>>

I am writing to you to ask whether you would be willing to take part in a research project being carried out in King's College Hospital. This is in collaboration with Professor Michael Kopelman at St Thomas' Hospital and is being done by a researcher, Ms Anneli Cassel.

We are asking you to contribute because your neurological condition, temporal lobe epilepsy, is sometimes associated with having difficulty with memory ability. We are interested in looking at whether, over time, people with temporal lobe epilepsy may forget things they are trying to remember faster than normal.

Taking part involves a visit to King's College Hospital for about two hours during which time we would ask you to take part in some tasks using your memory and other mental abilities. This would be followed by two telephone calls, one a day later and one a week later, to test your memory over a longer time period.

If you are interested in taking part Ms Cassel will contact you to provide further details about the study and send you a Participant Information Sheet. By expressing interest you are not obliged to take part.

We would be most grateful if you would fill in the slip indicating whether you are interested or not in taking part, and return it to me in the stamped and addressed envelope. It would be helpful if you were able to return the slip within two weeks of receipt of this letter, if possible.

Participation in the study is **completely voluntary** and you are free to withdraw at any time. This will in **no way** affect the care you receive at the hospital. Also, you do not have to provide a reason for withdrawing.

If you have any queries about this request, please contact us using the above telephone number, or you are welcome to write to us using the above address.

Yours sincerely,

Professor Robin Morris
Head of Clinical Neuropsychology

Memory Study: Response Sheet
Department of Clinical Neuropsychology, King's College Hospital

Your Name: .....

I agree to Ms Anneli Cassel contacting me to give further information about the study (please circle your response below).

AGREE / DISAGREE

Preferred Contact Number: .....

N.B.

- Agreeing to be contacted does not commit you to taking part in the study.
- If you do agree to take part, after a discussion with Ms Anneli Cassel and reading the Participant Information Sheet, you can withdraw your participation at any time. This will not affect your care at the hospital.
- If you do not agree to be contacted, this will not affect your care at the hospital.

Please place this sheet in the stamped addressed envelope provided for posting.

- With Thanks -

Guy's and St Thomas' NHS
NHS Foundation Trust

Professor Michael Koutroumanidis

Department of Neurophysiology and Epilepsies
3rd Floor, Lambeth Wing
St Thomas' Hospital
Westminster Bridge Road
London SE1 7EH

Tel: 020 7188 3954

<<Date>>

<<Recipient Address>>

Dear <<Recipient>>

I am writing to you to ask whether you would be willing to take part in a research project being carried out in the Department of Neurophysiology and Epilepsies at St Thomas' Hospital. This is in collaboration with Professor Michael Kopelman at St Thomas' Hospital and Professor Robin Morris at King's College Hospital and is being done by a researcher, Ms Anneli Cassel.

We are asking you to contribute because your neurological condition, temporal lobe epilepsy, is sometimes associated with having difficulty with memory ability. We are interested in looking at whether, over time, people with temporal lobe epilepsy may forget things they are trying to remember faster than normal.

Taking part involves a visit to St Thomas' Hospital for about two hours during which time we would ask you to take part in some tasks using your memory and other mental abilities. This would be followed by two telephone calls, one a day later and one a week later, to test your memory over a longer time period.

If you are interested in taking part Ms Cassel will contact you to provide further details about the study and send you a Participant Information Sheet. By expressing interest you are not obliged to take part.

We would be most grateful if you would fill in the slip indicating whether you are interested in taking part or not, and return it in the stamped and addressed envelope. It would be helpful if you were able to return the slip within two weeks of receipt of this letter, if possible.

Participation in the study is **completely voluntary** and you are free to withdraw at any time. This will in **no way** affect the care you receive at the hospital. Also, you do not have to provide a reason for withdrawing.

If you have any queries about this request, please contact us using the above telephone number, or you are welcome to write to us using the above address.

Yours sincerely,

Professor Michael Koutroumanidis
Lead Clinical Neurophysiologist and Neurologist

Memory Study: Response Sheet
Department of Neurophysiology, St Thomas' Hospital

Your Name: .....

I agree to Ms Anneli Cassel contacting me to give further information about the study (please circle your response below).

AGREE / DISAGREE

Preferred Contact Number: .....

N.B.

- Agreeing to be contacted does not commit you to taking part in the study.
- Receiving a phone call from Ms Anneli Cassel if you do not return this slip does not commit you to taking part in the study.
- If you do agree to take part, after a discussion with Ms Anneli Cassel and reading the Participant Information Sheet, you can withdraw your participation at any time. This will not affect your care at the hospital.
- If you do not agree to be contacted, this will not affect your care at the hospital.

Please place this sheet in the stamped addressed envelope provided for posting.

- With Thanks -

Appendix 5: Participant Information Sheet (for Patients)

Institute of Psychiatry at The Maudsley

KING'S College LONDON

South London and Maudsley NHS NHS Foundation Trust
King's College Hospital NHS NHS Foundation Trust
Guy's and St Thomas' NHS NHS Foundation Trust

Participant Information Sheet (for Patients)
Version 3.0, 20/05/13, REC Number: 13/LO/0399

Study title: Accelerated forgetting in people with TLE, TEA and/or MTL lesions

Principal Investigator: Miss Anneli Cassel
Co-investigators: Prof Michael Kopelman
Prof Robin Morris

Invitation

You are being invited to take part in the above research study. Before you make your decision it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

This document contains two parts:

***Part 1** explains to you the purpose of this study and what will happen if you take part.*
***Part 2** gives you more detailed information about how the study will be conducted.*

If you decide, after reading this information sheet, that you would like to participate in the study you will be asked to complete the consent form.

Thank you for reading this.

Part 1

1. What is the purpose of the study?

People with epilepsy, particularly temporal lobe epilepsy (TLE) and transient epileptic amnesia (TEA), often complain of memory difficulties. Despite this, many can perform normally on the measures we currently use to assess for memory problems. It may be that, in these cases, something called "accelerated forgetting" is happening. This means that some people may forget things faster than usual.

The purpose of this study is to see if this is the case. If so, we want to see if this faster forgetting is something only seen in people with epilepsy in the temporal lobes, or if it is also seen in people who have damage to the temporal lobes (without epilepsy). The findings from this study may go on to change the way we assess memory problems in clinics and the recommendations we make to people who are having memory problems due to faster forgetting.

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King's College Hospital NHS NHS Foundation Trust

Guy's and St Thomas' NHS NHS Foundation Trust

2. Why have I been invited?

You have been invited because you are a patient referred to one of the following services; the Department of Neurophysiology at St Thomas' Hospital, the Neuropsychiatry and Memory Disorders Unit at St Thomas's Hospital or Clinical Neurosciences at King's College Hospital. We are inviting all patients who are identified as having temporal lobe epilepsy, transient epileptic amnesia or have medial temporal lobe damage, and who do not meet our exclusion criteria, under the care of either Guy's & St Thomas' NHS Foundation Trust, South London and Maudsley NHS Foundation Trust or King's College Hospital NHS Foundation Trust to take part. We hope approximately 60 people will take part in the study in total.

3. Do I have to take part?

No! It is up to you whether you take part. If you agree to take part you will be given this information sheet to keep and be asked to sign a consent form. **If you decide to take part you are still free to withdraw at any time and without giving a reason**. This will not affect the standard of care you receive.

4. What will happen to me if I take part?

If you agree to take part;

- One of the members of the research team (a Trainee Clinical Psychologist) will organise a convenient time for you to attend an appointment at St Thomas' Hospital, King's College Hospital or the Institute of Psychiatry (whichever is more convenient for you). At this appointment, she will meet you and ask you to sign the consent form.
- At this appointment, which may take up to two hours to complete, we will be asking you to participate in a series of tasks looking at your memory and other mental abilities. Some tasks will be like puzzles and some will be using words. We will also ask you to take part in two learning tasks, one looking at stories and one looking at routes. You will be able to take breaks if you need to.
- Also at this appointment, we will ask you to fill out some questionnaires asking about your mood and memory. These will take approximately 10 minutes to complete.
- **If you wear glasses, you will need to bring them with you for the appointment.**
- At the end we will arrange a convenient time to call you at home the next day. For one of the tasks, you will need to look at some pictures and we will ask you whether you would prefer to look at them over the internet, on a CD or on paper. If you chose to be given the pictures on paper, you will be handed two labeled envelopes. **Please do not open these envelopes before you are contacted by the researcher.**
- One day later, at the time arranged at your assessment, you will receive a phone call from the researcher you met the previous day to continue asking questions about the tasks you learned. This phone call should last about 10-15 minutes. Depending on how you decided to look at the pictures, you will need to be either near a computer or have the unopened envelopes to hand. The researcher will also arrange a convenient time six days later, i.e. one week after you came to your assessment, to

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call you again.

- Six days later, at the time arranged during the previous phone call, you will receive another phone call from the researcher to continue asking questions about the tasks you learned. Again, this phone call should last about 10-15 minutes. Depending on how you decided to look at the pictures, you will need to be either near a computer or have the unopened envelopes to hand.
- If you have epilepsy, we will ask you to return your seizure diary to the research team after this final phone call, using the stamped and addressed envelope provided to you.

5. Will I be reimbursed for travel expenses?

Travel expenses (at standard fare rates), up to a value of £10, which you have had to pay to travel to and from the assessment visit will be reimbursed upon presentation of receipts.

6. What will I have to do?

We would like you to agree for us to access your medical records to collect data about your health, and your neuroradiological and/or neurophysiological results. We would also like you to agree to attend an appointment at your respective hospital, or the Institute of Psychiatry (whichever is more convenient for you). At this appointment we would like you complete a series of tasks to give us some background information about your mental abilities. Some of these tasks will be like puzzles and some will be using words. We would also like you to complete two learning tasks, one looking at stories and one looking at routes. There are four short questionnaires we would also ask you to complete at this appointment.

We would ask you to agree to be contacted one day and one week after this, for a phone-call that will last about 10-15 minutes. If you have epilepsy, we would also ask you to keep a seizure diary over that week.

There are no lifestyle restrictions required as a result of participating in the study.

7. What are the possible disadvantages and risks of taking part?

There are no risks to your health or any changes to your treatment if you agree to take part in this study. Assessments of neuropsychological functioning are not harmful or distressing, but some people can find them challenging or fatiguing, and so breaks will be provided.

There is a possibility that the results from the neuropsychological assessment may reveal some information that needs to be followed-up clinically. Because of this, we will ask your permission to share your results with your responsible clinician if there are any findings that require clinical follow-up. They will be able to contact you and make arrangements for the appropriate treatments and supports to be put in place.

If for any reason you feel uncomfortable whilst taking part, you are reminded of your right to

withdraw at any time. In addition, if you wish to talk to your consultant at any stage of the study, arrangements can be made.

8. What are the possible benefits of taking part?

By agreeing to take part in the study you will be contributing towards a better understanding of how memory works and the kinds of memory problems people with either damage or epilepsy in their temporal lobes have.

Although taking part in this study will not be of any direct benefit to you clinically, if during data collection we find anything that requires clinical follow-up, we will let your responsible clinician know of this finding so they can make arrangements with you for appropriate treatments and supports to be put in place.

9. What happens when the research study stops?

At the end of the research your care remains the same. We would like to have the opportunity to contact you with information regarding the overall findings of the study.

10. What if something goes wrong?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

11. Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

1. What will happen if I don't want to carry on with the study?

You can withdraw from the study at any point during the study without *any* impact on your clinical care. If you do decide to withdraw from the study, all paper data collected about you up to that point will be destroyed using a confidential shredder, and all information stored electronically will be securely deleted.

2. What if there is a problem?

Since this study is only recording information about you and asking you to complete tasks

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that look at memory and other thinking skills, it is very unlikely that something will go wrong. However if you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action against the NHS Foundation Trust but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you.

3. Will my taking part in this study be kept confidential?

All the information recorded will be strictly confidential and kept in accordance with the Data Protection Act 1998, and used only by clinicians and researchers working within the research team. Data from the study regarding you will be stored anonymously and any information about you that leaves the hospital will have your name and address removed so that you cannot be identified.

4. Will my responsible clinician be informed of my participation?

We will ask your permission for us to contact your responsible clinical at the hospital to inform them of your participation in the research study. We will also ask your permission to share the results of your neuropsychological assessment with them if there are any findings of clinical significance.

5. What will happen to the results of the research study?

When the study is completed we intend to publish the results in order to help other researchers and health care professionals increase understanding about accelerated forgetting rates in people with damage or epilepsy in the temporal lobes. You will not be named in any reports or results we publish.

6. Who is organising and funding the research?

This study is being conducted by academic staff and students at the Institute of Psychiatry (IoP), part of King's College London. It has been organised by a Trainee in Clinical Psychology, Anneli Cassel, supervised by Prof. Michael Kopelman and Prof. Robin Morris (King's College London). The research team is not being paid for including and looking after the patients taking part in the study. The IoP are sponsoring this study.

7. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed by the NRES London – City & East Committee.

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8. Contacts for Further Information

If you do require additional information, please use the contacts below:

For independent advice you can contact PALS (Patient Advice and Liaison Service) by visiting www.pals.nhs.uk or by contacting the PALS office at your hospital:

Guy's and St Thomas' Hospitals:

Patient Advice & Liaison Service, Patient Information Team, KIC, Ground floor, North Wing, St Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH

King's College Hospital:

Patient Advice & Liaison Service, Ground Floor, Hambledon Wing, King's College Hospital, Denmark Hill, London, SE5 9RS

For information about the study:

Prof. Michael Kopelman
Project Supervisor
michael.kopelman@kcl.ac.uk
020 7188 5396

Prof. Robin Morris
Project Supervisor
robin.morris@kcl.ac.uk
020 7848 0849

Anneli Cassel
Trainee Clinical Psychologist
anneli.cassel@kcl.ac.uk
020 7848 0223

Thank you for reading this.

You will be given a copy of the information sheet and a signed consent form to keep.

Appendix 6: Participant Information Sheet (for Controls)

Institute of Psychiatry at The Maudsley

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South London and Maudsley NHS NHS Foundation Trust
King's College Hospital NHS NHS Foundation Trust
Guy's and St Thomas' NHS NHS Foundation Trust

Participant Information Sheet (for Controls)
Version 3.0, 20/05/13, REC Number: 13/LO/0399

Study title: Accelerated forgetting in people with TLE, TEA and/or MTL lesions

Principal Investigator:	Miss Anneli Cassel
Co-investigators:	Prof Michael Kopelman
	Prof Robin Morris

Invitation

You are being invited to take part in the above research study. Before you make your decision it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

This document contains two parts:

***Part 1** explains to you the purpose of this study and what will happen if you take part.*
***Part 2** gives you more detailed information about how the study will be conducted.*

If you decide, after reading this information sheet, that you would like to participate in the study you will be asked to complete the consent form.

Thank you for reading this.

Part 1

1. What is the purpose of the study?

The purpose of this study is to see if a type of memory problem, where information is forgotten faster than usual, exists in people with particular conditions affecting their brain activity. This type of memory problem is called "accelerated forgetting". It may particularly affect those with damage to, or altered activity, in an area of the brain called the temporal lobes.

We would like to compare patients with conditions called temporal lobe epilepsy (TLE), transient epileptic amnesia (TEA) and temporal lobe damage with healthy controls to see if this "accelerated forgetting" occurs. This will help us understand this memory problem better and hopefully lead to better ways of assessing and managing it for the patients affected.

2. Why have I been invited?

In order for us to draw valid conclusions in our study, we need to compare the results of the forgetting measures in the patient groups with those in a healthy control group, i.e. people who do not have epilepsy, temporal lobe damage, other neurological or psychiatric conditions, and do not have any subjective memory complaints of their own.

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You have been invited as a healthy volunteer to be part of the control group.

3. Do I have to take part?

No! It is up to you whether you take part. If you agree to take part you will be given this information sheet to keep and be asked to sign a consent form. **If you decide to take part you are still free to withdraw at any time and without giving a reason**.

4. What will happen to me if I take part?

If you agree to take part;

- One of the members of the research team (a Trainee Clinical Psychologist) will organise a convenient time for you to attend an appointment at either St Thomas' Hospital, King's College Hospital or the Institute of Psychiatry (whichever is more convenient for you). At this appointment, she will meet you and ask you to sign the consent form.
- At this appointment, which may take up to two hours to complete, we will be asking you to participate in a series of tasks looking at your memory and other mental abilities. Some tasks will be like puzzles and some will be using words. We will also ask you to take part in two learning tasks, one looking at stories and one looking at routes. You will be able to take breaks if you need to.
- Also at this appointment, we will ask you to fill out some questionnaires asking about your mood and memory. These will take approximately 10 minutes to complete.
- **If you wear glasses, you will need to bring them with you for the appointment.**
- At the end we will arrange a convenient time to call you at home the next day. For one of the tasks, you will need to look at some pictures and we will ask you whether you would prefer to look at them over the internet, on a CD or on paper. If you chose to be given the pictures on paper, you will be handed two labeled envelopes. **Please do not open these envelopes before you are contacted by the researcher.**
- One day later, at the time arranged at your assessment, you will receive a phone call from the researcher you met the previous day to continue asking questions about the tasks you learned. This phone call should last about 10-15 minutes. Depending on how you decided to look at the pictures, you will need to be either near a computer or have the unopened envelopes to hand. The researcher will also arrange a convenient time six days later, i.e. one week after you came to your assessment, to call you again.
- Six days later, at the time arranged during the previous phone call, you will receive another phone call from the researcher to continue asking questions about the tasks you learned. Again, this phone call should last about 10-15 minutes. Depending on how you decided to look at the pictures, you will need to be either near a computer or have the unopened envelopes to hand.

5. Will I be reimbursed for travel expenses?

Travel expenses (at standard fare rates), up to a value of £10, which you have had to pay to travel to and from the assessment visit will be reimbursed upon presentation of receipts.

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6. What will I have to do?

We would like you to agree to attend an appointment at St Thomas' Hospital, King's College Hospital or the Institute of Psychiatry (whichever is more convenient for you). At this appointment we would like you complete a series of tasks to give us some background information about your mental abilities. Some of these tasks will be like puzzles and some will be using words. We would also like you to complete two learning tasks, one looking at stories and one looking at routes. There are four short questionnaires we would also ask you to complete at this appointment.

We would ask you to agree to be contacted one day and one week after this, for a phone-call that will last about 10-15 minutes.

There are no lifestyle restrictions required as a result of participating in the study.

7. What are the possible disadvantages and risks of taking part?

There are no risks to your health if you agree to take part in this study. Assessments of neuropsychological functioning are not harmful or distressing, but some people can find them challenging or fatiguing, and so breaks will be provided.

There is a possibility that the results from the neuropsychological assessment may reveal some information that needs to be followed-up clinically. If this is the case, we will ask your permission to share your results with your GP if there are any findings that require clinical follow-up. They will be able to contact you and make arrangements for the appropriate treatments and supports to be put in place.

If for any reason you feel uncomfortable whilst taking part, you are reminded of your right to withdraw at any time.

8. What are the possible benefits of taking part?

Taking part in this study will not be of any direct benefit to you clinically, although we hope that your participation will contribute towards a better understanding of how memory works and the kinds of memory problems people with either damage or epilepsy in their temporal lobes have.

9. What happens when the research study stops?

We would like to have the opportunity to contact you with information regarding the overall findings of the study.

10. What if something goes wrong?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

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11. Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

1. What will happen if I don't want to carry on with the study?

You can withdraw from the study at any point during the study. If you do decide to withdraw from the study, all paper and electronic data collected about you up to that point will be securely destroyed.

2. What if there is a problem?

Since this study is only recording information about you and asking you to complete tasks that look at memory and other thinking skills, it is very unlikely that something will go wrong. However if you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action against the NHS Foundation Trust but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you.

3. Will my taking part in this study be kept confidential?

All the information recorded will be strictly confidential and kept in accordance with the Data Protection Act 1998, and used only by researchers working within the research team. Data from the study regarding you will be stored anonymously and any information about you that leaves the hospital will have your name and address removed so that you cannot be identified.

4. Will my responsible clinician be informed of my participation?

We may ask your permission for us to contact your GP, to share the results of your neuropsychological assessment with them, if there are any findings of clinical significance.

5. What will happen to the results of the research study?

When the study is completed we intend to publish the results in order to help other researchers and health care professionals increase understanding about accelerated

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forgetting rates in people with damage or epilepsy in the temporal lobes. You will not be named in any reports or results we publish.

6. Who is organising and funding the research?

This study is being conducted by academic staff and students at the Institute of Psychiatry (IoP), part of King's College London. It has been organised by a Trainee in Clinical Psychology, Anneli Cassel, supervised by Prof. Michael Kopelman and Prof. Robin Morris (King's College London). The research team is not being paid for including and looking after the patients taking part in the study. The IoP are sponsoring this study.

7. Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed by the NRES London – City & East Committee.

8. Contacts for Further Information

If you do require additional information, please use the contacts below:

For independent advice you can contact PALS (Patient Advice and Liaison Service) by visiting www.pals.nhs.uk or by contacting the PALS office at one of the following hospitals:

Guy's and St Thomas' Hospitals:
Patient Advice & Liaison Service, Patient Information Team, KIC, Ground floor, North Wing, St Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH

King's College Hospital:
Patient Advice & Liaison Service, Ground Floor, Hambledon Wing, King's College Hospital, Denmark Hill, London, SE5 9RS

For information about the study:

Prof. Michael Kopelman	**Prof. Robin Morris**	**Anneli Cassel**
Project Supervisor	Project Supervisor	Trainee Clinical Psychologist
michael.kopelman@kcl.ac.uk	robin.morris@kcl.ac.uk	anneli.cassel@kcl.ac.uk
020 7188 5396	020 7848 0849	020 7848 0223

Thank you for reading this.

You will be given a copy of the information sheet and a signed consent form to keep.

Appendix 7: Consent Forms

Institute of Psychiatry at The Maudsley

KING'S College LONDON

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NHS Foundation Trust
King's College Hospital NHS
NHS Foundation Trust
Guy's and St Thomas' NHS
NHS Foundation Trust

CONSENT FORM (for Patients)

Study title: Accelerated forgetting in people with TLE, TEA and/or MTL lesions

Principal Investigator: Miss Anneli Cassel
Co-investigators: Prof Michael Kopelman
Prof Robin Morris

	Please Initial
1. I confirm that I have read and understand the information sheet dated 20/05/13 (Version 3.0) for the above study and have had the opportunity to ask questions.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I understand that sections of my medical notes may be looked at by responsible individuals from the research team where it is deemed relevant to my taking part in this research. I give permission for these individuals to have access to my data.	
4. I agree to the researcher informing my responsible clinician about my participation in the above study.	
5. I understand that data gathered from participation in the study will be confidential, **except** if information is uncovered during the assessment that requires further follow-up and support, I give consent for you to alert my responsible clinician so that I can receive the necessary treatment.	
6. I understand that data collected from me will be held anonymously and securely, in accordance with the Data Protection Act (1998).	
7. I agree to the researcher contacting me during the study to arrange times for the assessment to be carried out.	
8. I understand that I will be asked to attend hospital for a research appointment to complete a brief neuropsychological assessment, other learning tasks and complete questionnaires.	
9. I understand I will be asked to be contacted one day and one week after I complete the neuropsychological assessment for a 10-15 minute phone call.	

..... Name of Participant	..... Date	..... Signature
..... Researcher	..... Date	..... Signature

1 copy for patient; 1 copy for researcher; 1 copy to be kept with hospital notes

Consent Form, Version 1.0, 15/02/13, REC Number: 13/LO/0399 1

Institute of Psychiatry at The Maudsley

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South London and Maudsley NHS NHS Foundation Trust
King's College Hospital NHS NHS Foundation Trust
Guy's and St Thomas' NHS NHS Foundation Trust

CONSENT FORM (for Controls)

Study title: Accelerated forgetting in people with TLE, TEA and/or MTL lesions

Principal Investigator: Miss Anneli Cassel
Co-investigators: Prof Michael Kopelman
Prof Robin Morris

	Please Initial
1. I confirm that I have read and understand the information sheet dated 20/05/13 (Version 3.0) for the above study and have had the opportunity to ask questions.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I understand that data gathered from participation in the study will be confidential, **except** if information is uncovered during the assessment that requires further follow-up and support, I give consent for you to alert my GP so that I can receive the necessary treatment.	
4. I understand that data collected from me will be held anonymously and securely, in accordance with the Data Protection Act (1998).	
5. I agree to the researcher contacting me during the study to arrange times for the assessment to be carried out.	
6. I understand that I will be asked to attend hospital for a research appointment to complete a brief neuropsychological assessment, other learning tasks and complete questionnaires.	
7. I understand I will be asked to be contacted one day and one week after I complete the neuropsychological assessment for a 10-15 minute phone call.	

.....	.....	.....
Name of Participant	Date	Signature
.....	.....	.....
Researcher	Date	Signature

1 copy for participant; 1 copy for researcher

Service Evaluation Project

What do Relatives Want? Feedback about Family Support on an Inpatient Neurorehabilitation Ward.

Supervised by Dr Sarah Crawford

Abstract

This audit sought to gather feedback from relatives on an inpatient neurorehabilitation ward about: (i) satisfaction with family support on the ward currently; (ii) awareness of, and feedback about, the Brain Injury Information Group; and (iii) their education and support needs during inpatient rehabilitation. A novel semi-structured questionnaire was designed in collaboration with the multidisciplinary team. There was a 62.5% response rate following a four-week data collection period.

93.3% of respondents were satisfied with the family support available to them currently. Only 26.7% of respondents were aware that there had been a psychoeducation group run on the ward due to the length of time that had lapsed since the last group session, of which only one respondent had attended any of the sessions. Reasons for non-attendance included both practical and personal motives. 100% of respondents identified education and support needs, which would be optimally offered early during their relative's admission and continue throughout on a monthly basis, with the option for individual or group sessions provided.

The results of the audit were disseminated to the multidisciplinary team and recommendations for service development and future audit were discussed. Service implications included recommendations for information provision, future groups, identifying at-risk relatives and developing a 'tool-kit' for family support. Future audit of awareness of the Drapers Ward leaflet, relatives' expectations when their family member is admitted to the ward, and how the service is meeting relatives' needs is recommended to develop a greater understanding of what works for whom.

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1. Introduction

1.1 Acquired Brain Injury (ABI)

Acquired brain injury (ABI) is an umbrella term that refers to people who have had an "acute (rapid onset) brain injury of any cause" (Royal College of Physicians & British Society of Rehabilitation Medicine [RCP & BSRM], 2003, p. 7). The injury could be caused by trauma (e.g. road traffic accident, fall, assault), vascular accident (e.g. stroke, subarachnoid haemorrhage), cerebral anoxia, infection (e.g. meningitis, encephalitis), inflammation (e.g. vasculitis) or other toxic or metabolic insult (e.g. hypoglycaemia).

Prevalence figures regarding the epidemiology of ABI are variable due to the heterogeneity of the population (RCP & BSRM, 2003). In the UK, it is estimated that approximately 20 people under the age of 65 have strokes per 100,000 in the population per year (RCP & BSRM, 2003; Bamford et al., 1988). 229 to 275 people per 100,000 in the UK population have a traumatic brain injury (TBI) requiring hospitalisation per year (Tennant, 2005; RCP & BSRM, 2003), of which 25/100,000 have moderate to severe brain injury. 65 to 85% of these patients make a good physical recovery, although many continue to have cognitive, emotional, behavioural, psychosocial and/or occupational sequelae (Rao & Lyketsos, 2000; Morton & Wehman, 1995; Tennant, Macdermott & Neary, 1995; Colantonio et al., 2004).

There is considerable variation in prevalence nationally due to lifestyle, demographic and environmental factors including variation between: urban and rural areas, with greater incidence in London, the Shire counties, the Midlands and Northern urban areas (Tennant, 2005); gender, with approximately a 2:1 male to female ratio (Tennant, 2005; Greenwald, Burnett & Miller, 2003; Abelson-Mitchell, 2008); and age group, with a peak in TBI between 15 and 24 years (Murdoch & Theodoros, 2001; Abelson-Mitchell, 2008).

The functional deficits following an ABI are heterogeneous, occurring across a range of severity, and often depend on localisation of damage. Injuries may be focal, i.e. specific to a particular area of the brain, which can be the result of stroke

or trauma, or diffuse, which may arise from other causes or be secondary to a trauma (RCP & BSRM, 2003). Depending on the cause and location of injury, people with ABI may experience a range of cognitive, behavioural, emotional, communication and physical difficulties. Many ABI survivors with moderate to severe injuries live for several decades post-injury, thus often experience life-long disability as a result of their injury (Teasell, Aubut, Bayley & Cullen, 2012). They may depend on their family, services and other support networks to varying degrees for assistance with activities of daily living, occupation, social integration, and financial and legal matters (Teasell et al., 2012; Mazaux & Richer, 1998).

The need for acute, sub-acute and post-acute rehabilitation for those who require such services is well documented in the literature and national clinical guidelines (Department of Health [DoH], 2005; RCP & BSRM, 2003; Mazaux & Richer, 1998). Of those aged 16 to 74 who have a brain injury, it is estimated 36 people per 100,000 require rehabilitation (Tennant, 2005).

However, in optimising the long-term outcome of a person with ABI, there is increasing recognition of the role the family system plays in adjusting to living with a brain injury. Lezak (1988) stated that brain injury must be considered a 'family affair' due to the influences of the injury on both the individual and the wider family. The impact of ABI on family members and the importance of offering support to families as a routine part of rehabilitation are discussed further below.

1.2 Impact of ABI on Families

Following an ABI, families must go through a process of adjustment as the sequelae of brain injury affects not only the individual but also the whole family system (Webster, Daisley & King, 1999; Gan, Campbell, Gemeinhardt & McFadden, 2006). Relationships can be significantly affected and issues can arise due to a number of changes. These include adjusting to the neurobehavioural sequelae post-injury that can affect over 80% of survivors of ABI (Thomsen, 1974). Changes in personality, cognition and behaviour include lacking insight, being more disinhibited, irritable, emotionally labile, having rigid thinking, poor memory and concentration difficulties (Oddy, Humphrey & Uttley, 1978a; Levin, Benton & Grossman, 1982). These neurobehavioural changes in the injured individual have

been found to predict mental health status of relatives and level of family functioning, with neurobehavioural sequelae associated with increased anxiety and depression in relatives and poorer overall family functioning, which interact reciprocally with one another (Schönberger, Ponsford, Olver & Ponsford, 2010). The effects of brain injury can be long-lasting for relatives: many can experience significant anxiety and depression symptoms up to 10 to 15 years post-injury (Rappaport, Herrero-Backe, Rappaport & Winterfield, 1989; Thomsen, 1984; Brooks, 1991; Kreutzer, Gervasio & Camplair, 1994).

Relatives often report higher ratings of subjective burden and stress as a result of their relative's brain injury (Brookes, Campsie, Symington, Beattie & McKinlay, 1986; McKinlay, Brooks, Bond, Martinage & Marshall, 1981), which can be related to changes in lifestyle, relationship, occupation and community roles. This is evidenced in findings that a high proportion of spousal relationships end in either separation or divorce after brain injury (Webster et al., 1999; Wood & Yurdakul, 1997). Studies examining family functioning have also found that there is greater family dysfunction when a member of the system has a brain injury (Anderson, Parmenter & Mok, 2002; Testa, Malec, Moessner & Browt, 2006). Unhealthy family dynamics may be measurable as early as admission to rehabilitation, and are likely to remain stable or worsen over time (Testa et al., 2006; Winstanley, Simpson, Tate, & Myles, 2006). Sources of stress identified in family members include lack of information about brain injury and lack of psychological and social service support (Oddy, Humphrey & Uttley, 1978b).

However, as posited in family systems theory, each member of the family system interacts with one another in a reciprocal and interacting fashion, contributing to overall family functioning (Leif, 1993). Thus, not only do the changes experienced by an individual with ABI impact the wider family members and the family's general functioning, but the mental health, distress and burden of wider family members also impacts on the individual with an ABI. Unhealthy family functioning can have a negative impact on the individual with an ABI's neuropsychological functioning and long-term outcome (Lehan, Arrango-Lasprilla, de los Reyes & Quijano, 2012; Sander et al., 2002; Vangel, Rapport & Hanks, 2011; Gan et al., 2006). Conversely, better emotional status in caregivers is associated with better

occupational and social integration outcomes for people with a brain injury (Sander, Maestas, Sherer, Malec & Nakase-Richardson, 2012; Sady et al., 2010). These studies show that poor family functioning can be detrimental to a person with ABI's recovery, whilst healthy family functioning can aid it and result in positive outcomes.

1.3 Importance of Family Support after ABI

Considering how brain injury can have long-lasting negative effects not just for the individual but also the family around them, which can also affect the recovery and long-term outcome of the injured individual, it is not surprising that policy guidelines have increasingly stressed the importance of systematically addressing relatives' needs in rehabilitation (DoH, 2005; RCP & BSRM, 2003; Accident Compensation Corporation, 2006; Royal College of Physicians, 2012).

Family involvement in the rehabilitation process has been found to result in better outcomes for the individual with a brain injury (Chua, Ng, Yap & Bok, 2007; Sherer et al., 2007). Thus, enabling the family to cope with the consequences of ABI and increase their resilience also benefits the brain-injured individual. Boschen, Gargano, Gerber and Brandys (2007) critically appraised the literature of family interventions after ABI and found the evidence base lacking. Four randomized-controlled trials of interventions targeting family members of brain-injured individuals were identified, three of which offered educational interventions (Carnevale, Anselmi, Buischio and Millis, 2002; Sinnakaruppan, Downey & Morrison, 2005; Sanguinetti & Catanzaro, 1987) and one which compared two support groups, stress-management versus information provision (Singer, Glang & Nixon, 1994). Three of these studies found favourable results for the intervention group compared to a control group, although all lacked methodological rigour and had small sample sizes.

Even so, despite the possible benefit of including and addressing relatives' needs in rehabilitation, it is important that this is offered sensitively (Neurological Alliance, 2001). Some relatives may prefer to process the changes in their lives outside of the rehabilitation environment. Norup, Kristensen, Siert, Poulsen and Mortensen (2011) found that relatives with greater levels of anxiety sought and received

more structured support, both individually and in groups, during their relative's admission on a neurorehabilitation unit. They also acknowledged that some relatives preferred to adapt to the changes associated with brain injury themselves and may not find professional support helpful.

Literature examining relatives' reported needs following ABI include the need for: early, on-going, and comprehensive service delivery; information provision about the effects of brain injury, community resources and financial assistance; psychological support to empower hope, discuss feelings and receive support emotionally; advocacy; and to learn ways to feel connected socially (Leith, Phillips & Sample, 2004; Campbell, 1988). However, these samples investigating relatives' needs have been in outpatient settings and so may not be reflective of the service needs of families when their relative with an ABI is in an inpatient neurorehabilitation setting.

Considering the scarcity of evidence-based family interventions after ABI (Boschen et al., 2007) and lack of literature exploring relatives' needs during inpatient neurorehabilitation, there is a need to further our understanding of firstly, what these needs are during inpatient rehabilitation and secondly, how to provide support to meet the needs of relatives during sub-acute rehabilitation to aid them in their adjustment to the often chronic effects of ABI on caregivers.

1.4 The Royal Hospital for Neuro-disability

The Royal Hospital for Neuro-disability (RHN) is the oldest independent hospital and medical charity in the UK. It provides assessment, rehabilitation, treatment and long-term care services to adults profoundly disabled by ABI and degenerative neurological conditions. The hospital also cares for a number of military personnel who have had a brain injury whilst in active service. The RHN aims to provide holistic care to enable the person with neurological impairment to reach their full potential and enjoy optimum quality of life.

The rehabilitation services at the hospital are provided across five wards, which cater for patients across a range of brain injury severity; from those in persistent vegetative state to those transitioning to living independently in the community.

Drapers Ward, the focus of this report, is a specialist ABI ward for patients with severe injuries ranging from minimally conscious state (MCS) to full consciousness. There is a multidisciplinary team (MDT) made up of medical, nursing, social work and therapy staff. The therapy team includes psychology, occupational therapy, physiotherapy, speech and language therapy, dietetics, music therapy, and assistive technology. Patients are offered rehabilitation for a 12-week block, following which there is an external case review and further rehabilitation offered if clinically justified.

1.5 Rationale for Gathering Family Feedback

Based on evidence that psychoeducation groups for relatives were effective (Boschen et al., 2007), the therapy team on Drapers Ward had trialled a multidisciplinary Brain Injury Information Group (BIIG) over the previous eight months for relatives on the ward. The aim of this group was to improve relatives' understanding of acquired brain injuries and, subsequently, understanding for the rationale for some rehabilitation approaches.

However, turnout at the group sessions was low. Of the 15 sessions run over an eight month period, turnout did not exceed three relatives per session and for some sessions there was no attendance. It was hypothesised that perhaps the needs of the relatives on Drapers Ward, a sub-acute inpatient rehabilitation ward, were different from those who make up the current evidence base, which is largely sampled from outpatient settings (e.g. Boschen et al., 2007; Leith et al., 2004; Campbell, 1988).

Identifying needs through patient feedback, in order to respond and organise services based on local need, has been recommended as a national priority (DoH 2008; DoH, 2011). Using experience feedback cycles to develop services has been shown to provide rich information for service improvement and allows services to move towards collaborative, rather than prescriptive, practice (DoH, 2009). Considering the National Service Framework for Long-Term Conditions (DoH, 2005) recommends that family support is an integral component of high-quality rehabilitation for people with ABI, gathering feedback about the group and

furthering the team's understanding of relatives' needs on Drapers Ward was important to improve the services provided for relatives currently.

1.6 Aims of Current Survey

The current survey aimed to identify: (i) relatives' views about the BIIG (if they had a relative on Drapers Ward when the group was running), (ii) their satisfaction with the level of support they were currently receiving on the ward, and (iii) what information or support they would like to receive from the rehabilitation team.

The survey aimed to highlight areas of satisfaction with the BIIG as well as more general family support to feed back to the service, and also to highlight the areas that could be improved upon to guide service planning.

2. Method

2.1 Audit Approval

Approval for the audit was granted by the RHN Audit Committee.

2.2 Questionnaire Development

The questionnaire was developed by the author, with supervisor guidance, following a discussion with members of the Psychology team about the areas they wished to receive feedback on. The drafted questionnaire was then shared with members of the multidisciplinary team who had been involved in the BIIG, including: Speech and Language Therapy; Occupational Therapy; Physiotherapy; Dietetics; and Nursing. The responses from each discipline were then incorporated into re-drafts until an agreed version was reached. See Appendix 1 for the project questionnaire.

The final questionnaire was split into three sections: (i) awareness of the BIIG group; (ii) satisfaction of family support on the ward currently; and (iii) education and support relatives would like to receive.

2.3 Data Collection

The questionnaire was given to as many family members who were related to a patient on the ward as possible. The rationale for this was to gather opinions from as many members of the family system as possible; considering all family members interact with the patient and one another, and may have independent views on what kind of support they would like to receive (Boschen et al., 2007; Thompson, 2009).

Relatives were approached on Drapers Ward face-to-face. The rationale for the survey was explained to them, they were informed that participation was entirely voluntary and that declining would in no way affect their relative's on-going care. Relatives were given the opportunity to fill the questionnaire in with the author if they wished, but were otherwise informed they could fill in the questionnaire anonymously and return it to a box on the ward.

Data was collected over a four-week period during June and July 2013.

3. Results

3.1 Overview of Relatives Approached and Responders

3.1.1 Relatives Approached

From the ward of 20 patients, 24 family members were approached who were related to 15 of these patients. The relative's relationship to the patient, and corresponding patient demographic and clinical variables, are reported below in Table 1.

Further demographic questions were not included in the questionnaire considering it would be fairly easy to identify who the respondent was had these questions been included. Therefore, there was a team decision to keep the questionnaire as anonymous as possible to enable relatives to provide honest feedback.

Five patients' relatives were not approached. Reasons for their exclusion included relative(s) not visiting the patient during the working week (40%), relative(s) did not speak English and there was not the opportunity to use an interpreter (40%), and no relative(s) identified (20%).

Table 1: Relatives approached with the feedback questionnaire and corresponding patient variables

	Relatives approached N=24
Relationship to Patient	
Parent	10 (41.67%)
Spouse	4 (16.67%)
Sibling	8 (33.33%)
Daughter	2 (8.33%)
Patient Variables	N=15
Age:	
Mean	42.87
S.D.	17.91
Range	20 - 75
Gender:	
Male	11 (73.33%)
Female	4 (26.67%)
Type of injury:	
TBI	4 (26.67%)
Vascular (e.g. stroke)	9 (60%)
Infection / Encephalitis	2 (13.33%)
Age at injury:	
Mean	41.8
S.D.	18.16
Range	19 - 75
Time between injury and admission to RHN:	
Median	3 months
Inter-Quartile Range	3 – 4.5 months
Time between injury and admission to Drapers Ward:	
Median	5 months
Inter-Quartile Range	2.5 – 6.5 months
Patient admitted straight to Drapers Ward:	8 (53.33%)
Patient admitted to other wards in RHN before Drapers:	7 (46.67%)

3.1.2 Response Rate

Of the 24 questionnaires handed out, 15 were returned. The overall response rate was therefore 62.5%. Three respondents (20%) opted to complete the questionnaire with the author and so their responses were potentially identifiable. Even so, it was not possible to ascertain demographic or clinical variables about

those who returned the questionnaire in this manner as such questions were not included.

3.2 Questionnaire Structure

The questionnaire has been broken down into the following sections for presenting results: (i) satisfaction of family support on the ward currently; (ii) awareness of the BIIG; and (iii) education and support relatives would like to receive.

3.3 Satisfaction of Family Support on Ward Currently

93.3% of respondents either 'agreed' or 'strongly agreed' that they were satisfied with the family support available on the ward currently. One respondent (6.7%) reported 'disagreeing' with the amount of family support available. This respondent added qualitative feedback regarding their dissatisfaction with family support:

"communication about [my relative's] rehabilitation is a big problem between team members, and between the team and me"

Another respondent added that:

"a monthly (or periodic) family meeting with all professional areas to discuss improvements would be useful"

3.4 Awareness of BIIG Group

Four (26.7%) of the respondents were aware of the BIIG group that had been previously run on the ward. 10 (66.7%) were not aware of the group, and there was missing data from one (6.7%) respondent.

Of the 10 respondents who were not aware of the group, nine 'agreed' or 'strongly agreed' that the group sounded like a helpful service to be offered to them, whilst one 'disagreed' that it would be helpful.

3.4.1 Feedback From Those Who Were Aware of the Group

3.4.1.1 Attenders

Of the four respondents who were aware of the group, one respondent attended one of the sessions. They reported attending the Brain Injury Education session, and 'agreed' that they were happy with the length, content, day, and time of the session. They also 'agreed' that attending had been helpful in increasing their understanding about brain injury in general and how their relative's brain injury was affecting them.

This respondent reported that the most helpful aspect of the group was:

"telling me how I had to be patient. Understanding that sometimes the brain injury controls [relative] and he can't talk or remember"

They also reported the aspect of the group that could have been improved was that the:

"sessions were maybe too lengthy"

3.4.1.2 Non-Attenders

The remaining three respondents who were aware of the group did not attend any of the sessions. There were varied reasons for their non-attendance. Reasons ranged from the day of the week not being convenient (33.3%), time of day not being convenient (33.3%), that they would rather spend their time with their relative (66.7%), and that the content of the session was not of interest to them (33.3%).

Two of the respondents provided further qualitative feedback:

"I wanted to attend, but it was only the timing of the group - I was at work"

"most of what was talked about I already knew"

3.5 Education

3.5.1 Education Relatives Would Like to Receive

100% of respondents 'agreed' or 'strongly agreed' that they would like to receive education about brain injury. Further details about the content of education, mode of delivery and frequency and timing of sessions is described further below.

3.5.2 Content of Education Sessions

Figure 1 shows the different aspects of education respondents endorsed as areas of interest for them.

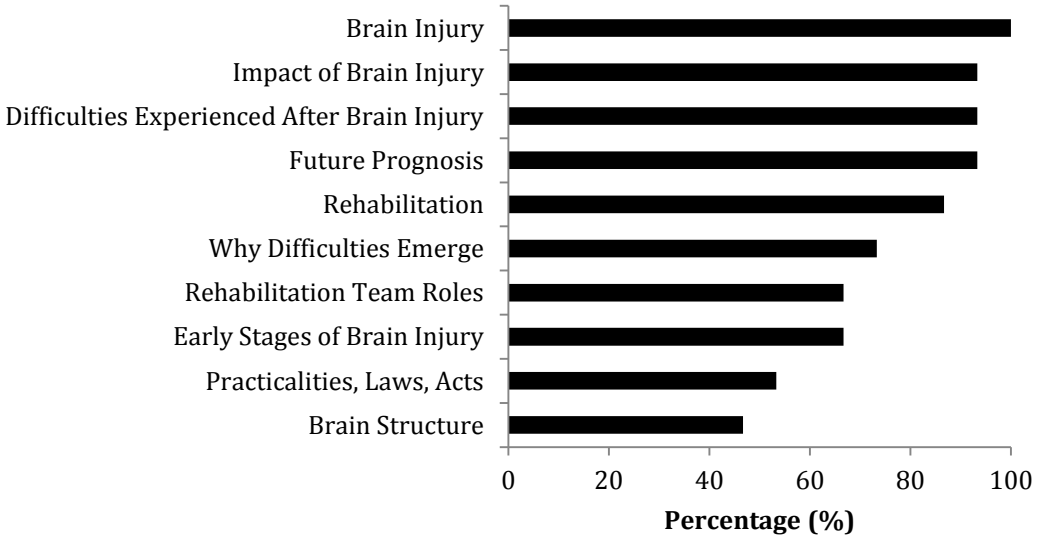

Figure 1: Content of education sessions endorsed as 'helpful' by respondents

100% of respondents reported wanting to find out about brain injuries, but less about the structure of the brain itself (46.7%). Other areas that more than 80% respondents reported as important included the impact of brain injury and the related day-to-day difficulties experienced by the individual (93.3% and 86.7% respectively), the future prognosis after severe brain injury (93.3%) and what rehabilitation is (86.7%).

Many also wanted to know more about why people with brain injuries have the difficulties they have (73.3%), the roles of different members of the multi-disciplinary team (66.7%), information about the early stages of brain injury to help make sense of the acute hospital experience (66.7%) and practical

information, including education about benefits, laws and Acts related to brain injury (53.3%).

Other qualitative comments respondents made included:

"what kinds of treatments there are for people with brain injury and the rationale for them"

"new technologies being developed, new therapies being researched (e.g. stem cell therapy)"

"how long it will be like this"

3.5.3 Mode of Delivery of Education Sessions

The majority of respondents rated receiving 1:1 education was of most importance to them (66.7%). 46.7% of respondents rated group-based education on the ward as next most important to receive, followed by group-based education across the hospital (46.7%). 86.7% of respondents rated receiving no further input from what they receive currently as least important. Figure 2 below shows the percentage rankings of the suggested modes of delivery.

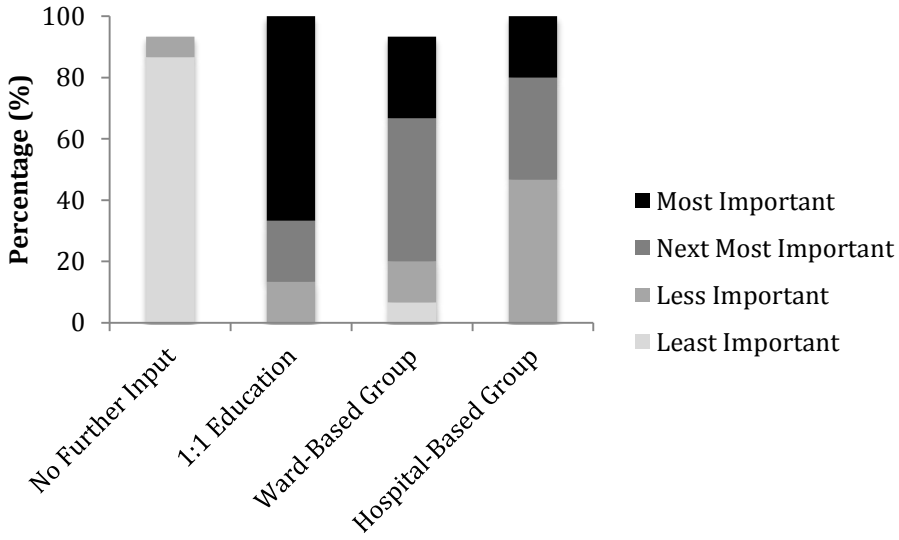

Figure 2: Rank order of suggested modes of delivery in which to receive education

The majority of respondents rated having conversations and discussions as how they would like to receive information (80%). Many also reported being provided leaflets as helpful (73.3%). Less popular modes of delivery included Powerpoint presentations (26.7%) and practical demonstrations (33.3%). One respondent gave qualitative feedback that it would also be helpful to have information available on the:

"RHN website so I know information I am learning is from a reputable source"

53.3% of respondents wished to receive very detailed information, followed by 46.7% wishing to receive some detail. Fewer wished to receive not much detail (20%) and no respondents wished for very little detail.

3.5.4 Frequency and Timing of Education Sessions

Figures 3 and 4 show the respondents preferred frequency and timing of education sessions during a relative's admission to the ward. The majority of respondents rated monthly sessions as most preferable (60%), with equal numbers responding that sessions at the beginning of their relative's admission (46.7%) and throughout (46.7%) would be most helpful.

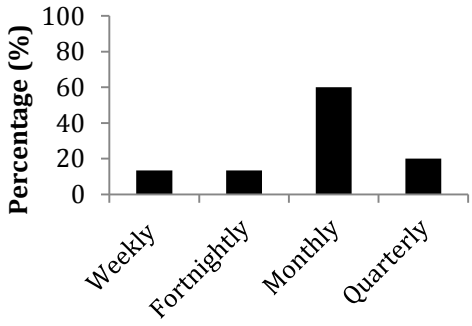

Figure 3: Frequency of education sessions endorsed as 'helpful'

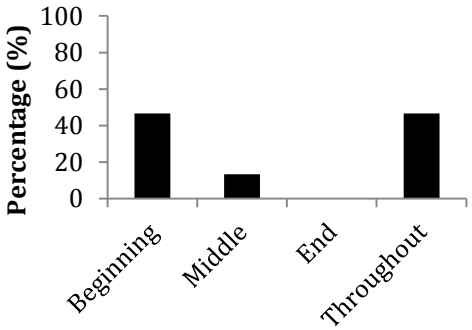

Figure 4: Time during admission of education sessions endorsed as 'helpful'

3.6 Support

3.6.1 Support Relatives Would Like to Receive

100% of respondents 'agreed' or 'strongly agreed' that they would like to receive support in coping with their relative's brain injury. Further details about the focus

of support, mode of delivery and frequency and timing of sessions is described below.

3.6.2 Content of Support Sessions

Figure 5 shows the different aspects of support respondents endorsed as areas of interest for them.

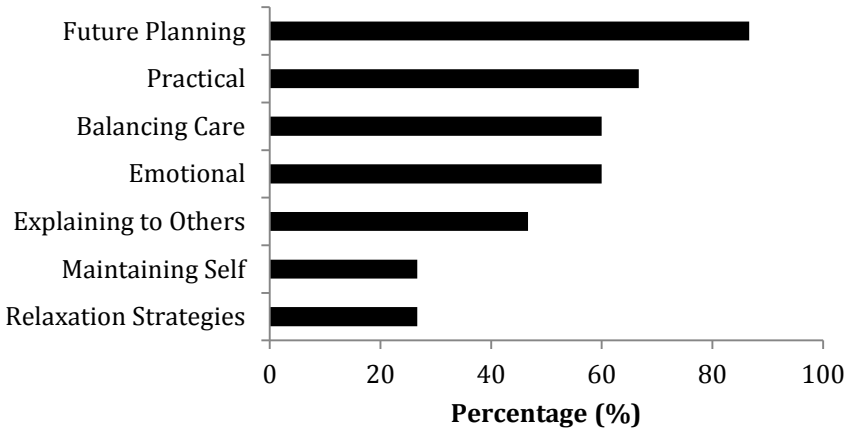

Figure 5: Content of support sessions endorsed as 'helpful' by respondents

86.7% of respondents reported wanting support with planning for the future, and linked to this 66.7% would like practical support, e.g. form filling, sign-posting etc. Respondents also reported wanting emotional support (60%) and support balancing care for their relative with their other responsibilities (60%).

Fewer than half of respondents reported wishing to receive support in explaining their relative's brain injury to others (46.7%), maintaining their sense of self (26.7%) and relaxation strategies (26.7%).

3.6.3 Mode of Delivery of Support Sessions

There was missing data from one respondent (6.7%) questioning the possible mode of delivery for support on the ward. The majority of respondents rated receiving 1:1 support was of most importance to them (66.7%). Following this, 66.7% of respondents rated having professionally facilitated group support as next most important. A peer facilitated group was rated as next most important by the majority of respondents (60%), with no further input rated as least important by

the majority of respondents (73.3%). Figure 6 below shows the percentage rankings of the suggested modes of delivery.

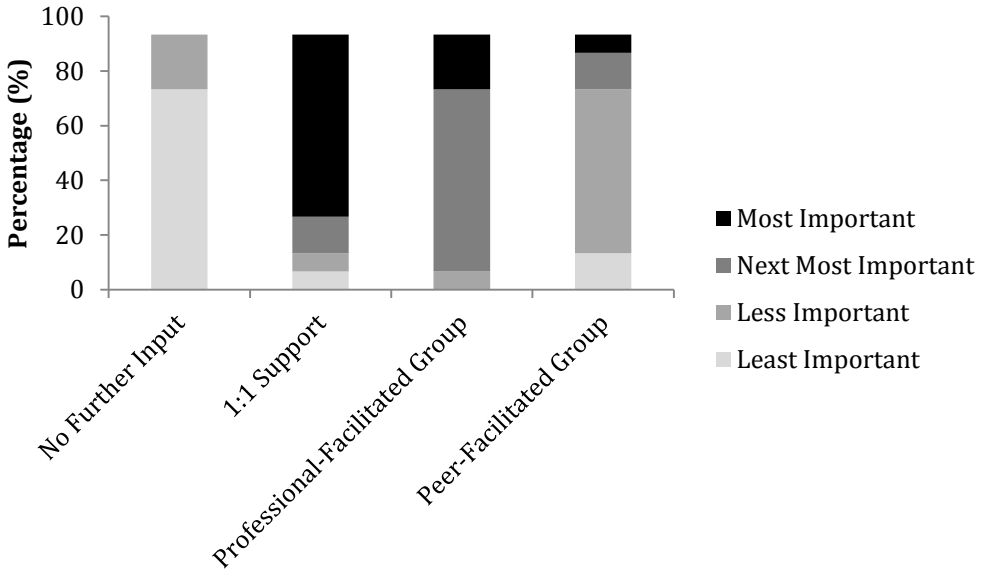

Figure 6: Rank order of suggested modes of delivery in which to receive support

3.6.4 Frequency and Timing of Support Sessions

Figures 7 and 8 show respondents preferred frequency and timing of support sessions during a relative's admission to the ward. The majority of respondents rated monthly sessions as most preferable (66.7%), with most stating that sessions throughout their relative's admission would be most helpful (53.3%).

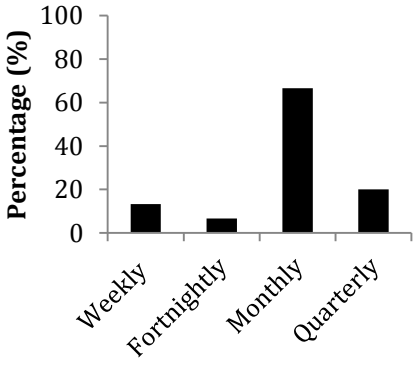

Figure 7: Frequency of support sessions endorsed as 'helpful'

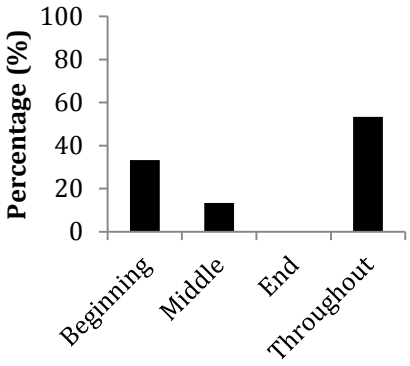

Figure 8: Time of support sessions endorsed as 'helpful'

3.7 Other Comments

Respondents were given the opportunity to provide further qualitative feedback at the end of the questionnaire. Three respondents (20%) provided comments:

"the main issue for me has been dealing with the different opinions within my family on how best to manage [relative's] care. This is very difficult. Also I sometimes feel angry when I come to visit and the staff speak to me rudely, say I cannot see [my relative] without respecting that I have come a long way to be here"

"at the moment I'm quite satisfied - [my relative's] getting all the care and attention they need"

"I had a meeting with various hospital staff and that has helped to understand a bit more about brain injury"

4. Discussion

4.1 Overview of Results

4.1.1 Section 1: Satisfaction on the Ward Currently

The results indicated that most respondents were satisfied with the amount of support they currently receive on the ward. Despite this positive finding, ratings of satisfaction are generally limited by demand characteristics, whereby respondents often rate their level of service satisfaction positively on questionnaire measures (Larsen, Attkisson, Hargreaves & Nguyen, 1979). This suggests that, although positive, any conclusions about relatives' satisfaction currently should be made with caution and are best interpreted in the context of the other findings reported below.

4.1.2 Section 2: Awareness and Feedback about BIIG

Few respondents were aware of the Brain Injury Information Group, but of those who were the majority did not attend the group. The reasons given for not attending implied that the timing of the group was not convenient, either due to practical (e.g. being at work) or personal reasons (e.g. wanting to spend time with their relative). Although one respondent had attended one session and gave largely

positive feedback, they also added that the session was perhaps too long. However, attending the session had met the group's aim of increasing the respondent's understanding of brain injury and how this related to their family member.

This suggests that a psychoeducation group run on an inpatient ward has the capacity to improve relatives' understanding of brain injury, similar to findings from the literature regarding family interventions after ABI (Boschen et al., 2007), although caution should be noted considering that this finding was only based on one respondent's feedback. Further research is necessary before concluding that psychoeducation groups on inpatient neurorehabilitation wards are helpful to relatives and their needs at this stage in their adjustment to ABI.

4.1.3 Section 3: Education and Support Needs

All respondents identified education and support needs. All respondents rated individual or group sessions as their most preferred modes of delivery, with no further input by the rehabilitation team as their least preferred option. This suggests that, although currently satisfied, all relatives on the ward would prefer there to be further structured sessions to facilitate their education about brain injury and rehabilitation, to offer support emotionally and practically in brain-injury related procedures and to aid in understanding and planning for the future.

Leaflets and discussions were identified as the most preferred methods of information provision. Fewer respondents rated Powerpoint presentations as helpful, indicating that this method may not engage relatives and could reduce their likelihood of attendance. It is possible that the formality of Powerpoint presentations and the didactic fashion in which such presentations are often given does not lend itself to inclusivity; and conversely, promotes prescriptive rather than collaborative service provision (DoH, 2009). This may alienate relatives from attending groups that utilise Powerpoint as their mode of information provision.

Respondents also rated monthly education and support sessions that started at the beginning of their relative's admission and continued throughout as most preferable. This is similar to the need identified by Leith et al. (2004) for there to be "early, continuous and comprehensive service delivery" for relatives following

ABI, albeit in a different setting. It also highlights the need for continual provision that can be accessed as needed. Norup et al. (2011) additionally found that more relatives sought professional support earlier in their relative's admission and that the hours of support decreased as time progressed, but was still available to them if necessary.

Interestingly, there appeared to be a theme amongst some qualitative responses that what mattered currently to relatives was feeling that their family member was receiving the best care and therapy available to them (e.g. "I'm satisfied…[my relative's] getting all the care and attention they need"). This focus on the patient, and ensuring their rehabilitation success, may give some insight into the needs of relatives at this stage in their adjustment. Perhaps during this sub-acute phase of recovery problem-solving, and avoidance-oriented, coping strategies may be more protective for relatives than emotionally-focused ones, which can be associated with greater emotional distress (Sander, High, Hannays & Sherer, 1997; Hanks, Rapport & Vangel, 2007). Even so, further research would be necessary to determine if this is the case, and to plan services accordingly.

4.2 Feedback to Service

A multi-disciplinary team meeting was organised with leads from the therapy and nursing teams invited to disseminate the results of the survey. The lead member from the psychology, occupational therapy, physiotherapy and dietetics team attended with apologies from speech and language therapy and nursing. Following the meeting, the feedback presentation was shared with wider team members on the shared ward drive. A time for ward staff to discuss the recommendations and plans for service development was added to the agenda of the ward's next Business Meeting.

4.3 Service Implications

4.3.1 Recommendations for Service Development

4.3.1.1 Information Provision

Considering the popularity of leaflets when selecting different options of information provision, it would be helpful for the ward to develop a range of

leaflets providing information about: (i) brain injuries; (ii) difficulties experienced after brain injury and why; (iii) rehabilitation; (iv) advice about capacity and decision-making (including information about Lasting Power of Attorney and Court of Protection procedures); and (v) signposting to other services. Addressing these areas has also been found to be important in other research investigating relatives' needs (e.g. Campbell, 1988).

These leaflets could be used by professionals to supplement discussions they have with family members to aid consolidation of information, subsequent recall and satisfaction with the service (Johnson, Sandford & Tyndall, 2003). Sinnakaruppan et al. (2005) found that when caregivers were provided educational pamphlets, in addition to information sessions, their scores on depression measures improved. Booklet provision as a method to provide education about brain injury and rehabilitation has been incorporated into other inpatient neurorehabilitation settings, in addition to verbal presentations, although outcomes have not been evaluated as yet (Foster et al., 2012). These findings and suggestions provide further incentive for the possible benefit of developing a pack of leaflets on Drapers Ward to supplement other aspects of family support, which could also be available on the hospital's website to increase accessibility (see Newby & Groom, 2010).

4.3.1.2 Future Groups

The lack of success of the BIIG may have been related to its mode of delivery; information was presented didactically in a universal, dose-response pattern. Psychoeducation groups about brain injury can help families make sense of their relative's difficulties but information must also be framed in ways that account for families appraisals and meanings associated with brain injury (Yeates, Henwood, Gracey & Evans, 2007). It may be that future groups planned on the ward could be more relative-led, with options of receiving education, peer support or sense-making based on needs identified in the lead up or during the session (Yeates, 2009).

It may also be helpful to avoid or minimise the use of Powerpoint to encourage collaboration rather than instruction. Considering that understanding about brain

structure was not regarded as important for relatives to learn about, provision of such information may be useful only when embedded into information about brain injury. Often, information about brain structure precedes information about injuries but this order may result in lost interest from relatives and difficulty applying such information to their relative.

Accounting for the practicalities of the ward environment also need consideration. For instance, there are visiting hours during which relatives can visit and they may be travelling a long distance. Groups need to be planned to minimise any practical constraints, e.g. offering sessions outside of working hours, when their relative is busy or in bed, and at a frequency that does not overwhelm relatives but also encourages attendance. Monthly sessions were identified as most preferred, thus it may be more helpful to run groups monthly to encourage greater attendance, rather than the fortnightly sessions that were running previously.

4.3.1.3 Identifying Relatives At-Risk of Distress

Holding a family meeting early in the rehabilitation process may be helpful in identifying relatives who are in need of family support. Such a meeting could provide rich information for the professional team in future work with the patient and family and also allow families to feel listened to (Yeates, 2009). Considering the majority of respondents would prefer to have education and support at the beginning of their family member's admission, it may be helpful for relatives to have an individual session with a member of the professional team early in the rehabilitation process. This meeting could involve discussions about the family's needs, expectations about rehabilitation, information about brain injury, and administration of measures of coping and distress. Considering that relatives who score highly on measures of anxiety have been found to receive more support during inpatient rehabilitation (Norup et al., 2011) it may be that the use of formal outcome measures could identify those relatives at-risk of poor coping, and thus have a greater need for professional support. It may also be necessary to offer staff training opportunities to increase their confidence with family work (Foster et al., 2012).

4.3.1.4 Developing a 'Tool-Kit' for Family Support

Based on the audit findings and national clinical guidelines (DoH, 2005; RCP & BSRM, 2003) it would be beneficial for the team to develop a comprehensive protocol for engaging and collaborating with families in rehabilitation on Drapers Ward. This would require further work to identify local needs and develop ways of how best to meet these needs, bearing in mind the heterogeneity of the ABI population and the families surrounding them. However, other rehabilitation practices have successfully developed such protocols (e.g. Yeates, 2009; Foster et al., 2012) that account for different rationales, types of liaison, aims of interventions and methods of provision at different times during the rehabilitation journey. This would provide the team with a 'tool-kit' to draw from in relation to family support and allow for a more operationalized, rather than ad-hoc, service provision for relatives.

4.3.2 Recommendations for Future Audit

4.3.2.1 Hospital Leaflets

When patients are admitted to RHN, their relatives receive a pack of information about the hospital. Included in this pack, if the patient is being admitted to Drapers Ward, is a leaflet about the ward, the rehabilitation team on the ward, and what the relative can expect over the coming 12 weeks. After analysing the results in this current audit, information provided in leaflet form and information about rehabilitation were identified as the most helpful resources relatives would like, which seemed ideally served by this leaflet already in circulation. However, in discussions at the feedback to service meeting, some therapy staff raised questions about whether relatives were receiving the leaflets about Drapers Ward in their information pack and whether the leaflets advertised in the communal area of the ward were noticeable enough. Further enquiry resulted in discovering that the Drapers Ward leaflet was not being circulated in the arrival information pack and the communal leaflets had been taken away following a health and safety incident. Therefore, future auditing of (i) awareness of the leaflet, (ii) receipt of the leaflet in the information pack and (iii) helpfulness of the leaflet would be beneficial to determine if this is a useful source of information for relatives when their family member is admitted to the hospital.

4.3.2.2 Relatives' Expectations

It is possible that current satisfaction ratings were related to wider expectations about the service, including the care their relative was receiving and other patient and relative characteristics. The relationship between satisfaction and expectations has been documented in the literature (e.g. Linder-Pelz, 1982), but was unfortunately not assessed currently. The importance of addressing relatives' expectations early in the rehabilitation process has been noted to be important in subsequently meeting relatives' needs (Hanks et al., 2007; Foster et al., 2012). If expectations are not adequately addressed both families and professionals can feel frustrated. This can lead to these families being labelled as a 'problem', thereby limiting collaboration between the team and relatives during rehabilitation in a vicious cycle (Yeates, 2009). Therefore, measuring expectations in future satisfaction audits may be useful to ensure services are targeted appropriately.

4.3.2.3 Meeting Relatives' Needs

This questionnaire aimed to identify relatives' education and support needs but it did not aim to discover if these needs were being met. The majority of respondents rated being satisfied generally with the amount of support they currently received and some gave qualitative feedback suggesting they were satisfied (e.g. "I've only been here two weeks…can't fault it"). However, respondents also consistently stated that they would like further structured education and support in addition to what they receive now. It may be that some relatives' needs are being met with current service provision, whilst others are not, and so it would be beneficial to not only identify needs but also understand how they are best met. Further audit or focus groups could help develop a greater understanding about how different needs are best met on the ward in future.

4.4 Limitations

4.4.1 Research Method

The use of a quantitative, fixed-choice, method may have masked any potential critical comments respondents may have made had questions been open-ended; thus, this format of questioning may have resulted in the generally positive responses that were gathered currently (Carr-Hill, Dixon & Thompson, 1989). Although there was some opportunity to add comments in the current

questionnaire, few respondents provided qualitative feedback (perhaps due to the questionnaire's length). It may have been more useful to have used a qualitative method, e.g. semi-structured interviews or focus groups to encourage elaboration of, and complexity in, responses (Williams, Coyle & Healy, 1998; Williams, 1994). This may have resulted in richer information being gleaned and themes associated with support needs identified, which may have allowed for the complexities of relatives' needs to be accounted for more comprehensively in future service development.

4.4.2 Methodological Criticisms

4.4.2.1 Questionnaire Structure

The finalised questionnaire was longer than anticipated because of the amount of information regarding the BIIG, education and support needs that was necessary to gather. This may have deterred some of the relatives approached from responding, considering that longer questionnaires have been found to reduce response rates in previous research (Iglesias & Torgerson, 2000). Perhaps there would have been more respondents or, of those who did respond, more may have provided qualitative feedback if the questionnaire had been shorter. It may have also been useful to have involved relatives during the questionnaire development stage. This may have prioritised aspects of the questionnaire most relevant to them rather than the focus currently on what professionals thought were most important (Cang, 1989). This may have improved that applicability of the questionnaire to relatives' needs and increased response rates (Gauld, Smith & Kendall, 2011; Thornicroft & Tansella, 2005).

Additionally, considering the heterogeneity of the ABI population and their families, Boschen et al. (2007) recommended that research investigating family interventions should clearly characterise its recipients. This recommendation could also apply to research investigating relatives' needs as there may be differences in relation to what support is needed and when, dependent on relatives: (i) demographics, (ii) role within the family, and (iii) injury information about the person with ABI (e.g. severity, nature of impairments, time since injury). This information was not gathered currently as there was a team decision to

prioritise anonymity of respondents, in the hope of promoting honest feedback, over gathering of demographic information. However, considering the literature surrounding individual, demographic and injury-related variables in family functioning after brain injury (Hanks et al., 2007; Gan et al., 2006; Ergh, Rapport, Coleman & Hanks, 2002; Verhaeghe, Defloor & Grypdonck, 2005) it is likely these variables may have an impact on the need and format of family support to be provided. It would be helpful for future audits and research to document these variables to determine information about what is helpful for whom.

4.4.2.2 Sampling

The methodology of the current survey was also limited due to the use of convenience sampling. Considering questionnaire distribution was only carried out during the working week, relatives were missed who could only visit their relative at the weekend. Their views regarding their needs was not gathered, and it may be that their needs are greater than those relatives who are able to visit during the week and seek out therapy staff for advice when it is needed. Additionally, those relatives where English language proficiency was limited were also not approached due to the inability to utilise interpreters for the current audit. Again, it is likely their needs for information and support are not met to a greater extent than relatives who can speak to staff in a shared language. Therefore, the results of the current audit were not representative across all families on the ward. Considering the ward consists of a diverse cultural and ethnic population, service development based on family feedback may be at risk of developing ethnocentrically if the needs of all relatives, regardless of language proficiency, ethnicity, culture or race, are not addressed.

4.4.2.3 Response Bias

Although the response rate in the current survey is higher than response rates in other survey research (Harrison & Cock, 2004), there may still be a bias amongst those who returned the questionnaire. Stallard (1995) found that levels of dissatisfaction were higher among non-responders to a postal questionnaire, perhaps because of a negative experience with the service. Thus, it may be that the positive responses received currently were related to characteristics of the respondents who chose to complete the questionnaire. Relatives who chose not to

respond to the questionnaire currently may be those with greater dissatisfaction with the service generally.

4.4.3 Timing of Data Collection

The rationale for gathering family feedback was borne out of recognition that the BIIG had not been successful and so feedback from relatives would provide helpful information as to why this was in order to aid service development. However, three months had passed between the last BIIG session and data collection. This meant that few respondents were even aware of the group to provide feedback: thus, limited information could be gleaned or conclusions drawn from their responses. Their responses may also have been subject to recall bias considering the amount of time that had passed. Ideally, feedback about the group should have been collected immediately or shortly after the sessions were held to minimise risk of recall bias (DoH, 2009) and to increase the response rate of respondents aware of the group.

4.5 Leadership

When starting my placement at RHN I was interested in what family support was available on the ward as I had previous experience working with families of people with brain injury. I had co-facilitated a relatives group in a community brain injury team prior to training, which had resulted in successful outcomes in easing relatives' distress and increasing their understanding about brain injury. I was interested in why there had been less success with such a similar group format in my current placement setting: perhaps families were at a different stage of adjustment with different needs or perhaps it was due to more practical considerations such as the timing and format of the group. This prompted discussions about the viability of carrying out an audit gathering feedback about the BIIG and assessing wider relative needs within the Psychology and local audit teams, which was received favourably. After discussing the project with the wider rehabilitation team, who were also very keen for such an audit to take place, I was able to begin carrying out the evaluation. I was involved and took a lead in all project stages: identifying a research question; questionnaire development; data collection; data analysis and dissemination to the service. Unfortunately, due to my

placement ending I was not able to be involved in applying the survey findings to service development.

5. Summary

The current audit sought to gather feedback about a psychoeducation group for relatives and to identify the local needs of relatives on Drapers Ward, an inpatient neurorehabilitation facility at the Royal Hospital of Neuro-disability. A semi-structured questionnaire was used to gather this feedback from as many relatives who could be identified during a four-week data collection period. 62.5% of the relatives approached returned the questionnaire, although only 26.7% of these respondents were aware of the group due to the length of time that had lapsed since the last group session.

Respondents reported a need for education and support during their relative's inpatient admission. This provision would be best serviced with individual families and through groups run on the ward, certainly at the beginning of their relative's admission but ideally continuing throughout their stay. Despite the low attendance at the previously run ward-based group this should not deter therapists from adopting a similar group in the future. Reasons for the previous BIIG's low attendance may have been due to its didactic format and practical limitations that could be modified in future groups. For instance, offering a more relative-led, discussion-based forum with educational components provided as necessary may be more engaging for relatives. Development of leaflets that can be circulated to relatives, based on individual needs, was also highlighted as a useful method of information provision in the current audit that has also received support in other research (e.g. Foster et al., 2012; Johnson, Sandford & Tyndall, 2003; Sinnakaruppan et al., 2005).

The findings from the current audit largely support previous research investigating what families needs are in rehabilitation and how best to meet these needs (Campbell, 1988; Foster et al., 2012; Yeates, 2009; Leith et al., 2004). These needs include: early and continual service provision; offering different family support services based on individual needs; responding flexibly to changes in needs; education about brain injury and rehabilitation to normalise each relative's

experience; and psychological support to reduce stress and promote adaptive coping.

Service findings and recommendations were disseminated to the multidisciplinary rehabilitation team currently, and further plans were made to discuss how best to address these needs within available clinical resources. Further audit and outcome measurement will ultimately be necessary to determine if any changes to service provision are helpful for relatives and their family member's rehabilitation outcome. It is not likely there will be any one approach that is helpful to all relatives, due to the uniqueness of each family on the ward. However, by devoting resources to development of a 'tool-kit' for family support the ward will be in a better position to recognise individuals' needs and possible ways to meet them. This may then reduce some of the negative sequelae associated with ABI and optimise the rehabilitative outcome for the brain-injured individual.

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7. Appendices

Appendix 1: Family Feedback Questionnaire

Family Feedback Questionnaire about Family Support on Drapers Ward

Drapers Ward would like to improve the support we give to family members of patients on the ward.

We would really appreciate your feedback about:

1) The Brain Injury Information Group that we ran from August 2012 to March 2013. You may not have heard about it, but this does not matter as we also would like to hear your feedback regarding the other points below.

2) The family support currently available on the ward.

3) What you would like to receive in terms of support from staff.

This questionnaire may take about 10 minutes to fill in. If you would like to fill it in anonymously, there is a box called "Family Support Feedback" on the reception desk on Drapers Ward that you can return the questionnaire to. If you would like help to fill in the questionnaire, please let Anneli Cassel, Trainee Clinical Psychologist, know and she will be happy to help fill in the questionnaire with you. Whichever way you choose to fill in the questionnaire, there will be no identifying information in your responses; your answers will remain anonymous.

We hope to take on board comments you make to improve the support we give to you, as the families of patients on the ward.

Thank you for your time!

1

Section 1: Feedback about the Brain Injury Information Group

Part A: Awareness of Group

1:1 Were you aware that the ward was running a Brain Injury Information Group for the relatives of patients on Drapers ward?

Yes ☐ No ☐

If you answered Yes, please move to question 1:3.
If you answered No, please answer the next question and then move onto Section 2.

1:2 Does the group sound like something you would find helpful to attend?

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

Please now move to "Section 2: Family support available on the ward" on page 5.

1:3 How did you find out about the group?

Staff member ☐ Poster ☐ Other relatives on the ward ☐ Other .....

1:4 Did you attend any of the sessions?

Yes ☐ No ☐

If you answered Yes, please complete Part B.
If you answered No, please complete Part C.

Part B: Feedback from those who attended

Please only complete this section if you attended one or more of the Brain Injury Information Group's sessions.

1:5 How many sessions did you attend?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

1:6 What was the content of the session(s) you attended?

Brain Injury Education ☐
Physical Presentation ☐
Cognition ☐
Nutrition & Swallowing ☐
Communication ☐

Thinking about the session(s) you attended:

1:7 I was happy with the length of the session(s).

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:8 I was happy with the content included in the presentations.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:9 I was happy with the day of the session(s).

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:10 I was happy with the time of the sessions(s).

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:11 Attending the session(s) was helpful.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:12 Attending the session(s) increased my understanding about brain injury generally.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:13 Attending the session(s) helped me understand more about my family member's brain injury.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

If you attended more than one session of the group, please continue from the next question.
If you attended one session, please move to question 1:16.

1:14 I was happy with different professionals running the different sessions.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:15 I was happy that the content in the different sessions was not repeating what I had learned in a previous session.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:16 In your opinion, what was the best thing about the group?

1:17 In your opinion, what did you think could be improved?

Now move to "Section 2: Family support available on the ward"

Part C: Feedback from those who decided not to attend

Please only complete this section if you were aware of the group, but decided not to attend.

1:18 The day of the week was not convenient for me.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:19 The time of day of the session was not convenient for me.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:20 I would rather spend my time with my family member.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:21 The content of the session(s) was not applicable to me and my care for my family member.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:22 The content of the session(s) was not of interest to me.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

1:23 If you have any other comments about why you decided not to attend, please describe further below.

Section 2: Family support available on the ward

2:1 I am happy with the amount of professional team involvement there is for families on the ward.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

2:2 Please describe further anything that you would like to be different about family support available on the ward currently.

Section 3: What you would like to receive from staff as a family member

Part A: Education

The following section asks about *education about brain injury* you may like to receive.

3:1 I would like there to be formal brain injury education sessions for families.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

There are a number of ways we could develop the education we give families of patients on Drapers Ward.

3:2 Please rank order (with 1 being your most preferred to 4 being your least preferred option) what you would like to receive.

No further team input beyond what is currently being provided ☐

Individual one-to-one time with professionals involved in my family member's care to provide me with information ☐

Group-based education for families on the ward ☐

Group-based education for families across the hospital ☐

Other:……

……

3:3 What kinds of information would you like to receive? Please tick all that apply.

Education about the brain, including its structure and function
e.g. information about the different lobes ☐

Education about different types of brain injuries
e.g. what happens when someone has a stroke or traumatic brain injury ☐

Education about the impact of brain injuries
e.g. how different parts of the brain are affected by injury ☐

Examples of the difficulties people have after a brain injury e.g. difficulties with memory, talking, understanding others, eating, swallowing, walking	
Explanations of why people have difficulties after a brain injury i.e. why people have the above difficulties after different brain injuries	
Information about what the future is like for someone with a brain injury e.g. what you might expect to change / stay the same as time goes on	
What we do as a rehabilitation team to help people after a brain injury i.e. how rehabilitation can help improve day to day life for someone with a brain injury	
Explanations of different team members roles on the ward i.e. information about what different therapists do and why	
Information about the early stages of a brain injury e.g. what happened and why just after the injury happened (i.e. when your family member was in an acute hospital)	
Information about practicalities and legal jargon e.g. Lasting Power of Attorney, Court of Protection, Mental Capacity Act	

Other:……

……

3:4 How would you like this information to be given to you?

Powerpoint presentations	
Practical demonstrations	
Discussions / Conversations	
Leaflets	

Other:……

……

3:5 How detailed would you like the information given to you?

Very detailed (I want lots of technical knowledge)	
Some detail (I want to get a bit of technical knowledge)	
Not much detail (I want to know a bit more than the basics/what I could read in books or online)	
Very little detail (I want just enough to get the basics)	

3:6 If you would like structured education sessions, how often would you like this to be offered to you?

Weekly ☐ Fortnightly ☐ Monthly ☐ Quarterly (once every 12 weeks) ☐

3:7 When would be the best time during your family member's admission for you to receive this kind of information?

Beginning ☐ Middle ☐ End ☐ Throughout ☐

Part B: Support

The following section asks about *support* you may like to receive.

3:8 I would like there to be support available for families.

Strongly Agree ☐ Agree ☐ Disagree ☐ Strongly Disagree ☐

There are a number of ways we could develop the support we give families of patients on Drapers Ward.

3:9 Please rank order (with 1 being your most preferred to 4 being your least preferred option) what you would like to receive.

No further team input beyond what is currently being provided	
Individual one-to-one support with an identified member of the professional team	
Group-based support facilitated by a professional member of the ward team	
Peer support, e.g. dedicated space for families to meet and support each other without professional involvement	

Other:……

……

3:10 What kinds of support would you like to receive or focus on? Please tick all that apply.

Emotional support i.e. forum to discuss emotional impact of your relative's brain injury	
Practical support e.g. benefits, form filling	
Strategies and tips to help when feeling stressed e.g. relaxation strategies	
Support in maintaining your sense of self and independence	
Support in getting the balance right i.e. caring for your relative in hospital vs everything else	
Support in understanding and planning for the future	
Advice on how to explain your relative's brain injury to others e.g. ways to describe, information to include	

Other:……

……

3:11 If you would like there to be support sessions, how often would you like this to be offered to you?

Weekly ☐ Fortnightly ☐ Monthly ☐ Quarterly (once every 12 weeks) ☐

3:12 When would be the best time during your family member's admission for you to receive this kind of support?

Beginning ☐ Middle ☐ End ☐ Throughout ☐

Section 4: Any Further Comments

Please make any further comments you have about the support you are currently receiving on the ward, what you would like to receive, and feedback on the Brain Injury Information Group below.

Thank you very much for taking the time to complete this questionnaire, you answers are greatly appreciated.

Please return to the box named "Family Support Feedback" on the reception desk on Drapers Ward or hand to Anneli Cassel, Trainee Clinical Psychologist.